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Design, synthesis and biological evaluation of flavonoids salicylate derivatives as potential anti-tumor agents

Xiangping Deng[a,1], Zhe Wang[a,1], Juan Liu[a], Shujuan Xiong[a], Runde Xiong[a], Xuan Cao[a], Yanming Chen[b], Zheng Xing[a], Guotao Tang[a,*]

[a]Institute of Pharmacy and Pharmacology, Hunan Province Cooperative Innovation Center for Molecular Target New Drug Study, University of South China, Hengyang, China,

[b]Mu Dan Jiang You Bo Pharmacertical Co.Ltd, Mudanjiang, China

*Corresponding Author: Dr. Guotao Tang, Ph.D.

Corresponding author at：

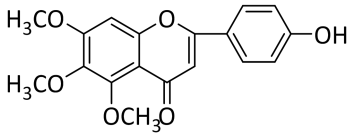
Guotao Tang, Institute of Pharmacy and Pharmacology, University of South China, Hengyang, Hunan, 421001, People's Republic of China.

E-mail adress: tgtzq@163.com

[1] These authors contributed equally to this work.

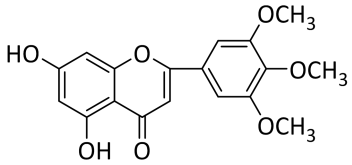
1. Experimental Section

1.1 Synthesis of 5,7-dihydroxy-2-(3,4,5-trimethoxyphenyl)-4H-chromen-4-one (2)



Golden powder, yield: 36%. Mp:194-195 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.4 Hz, 2H), 6.88 (d, *J* = 8.5 Hz, 2H), 6.73 (s, 1H), 6.53 (s, 1H), 5.11 (s, 1H), 4.24 (s, 3H), 3.96 (s, 3H), 3.81 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 181.26 (s), 163.89 (s), 161.79 (s), 158.01 (s), 151.50 (s), 146.44 (s), 136.51 (s), 133.41 (s), 124.71 (s), 116.17 (s), 112.64 (s), 107.34 (s), 90.59 (s), 77.37 (s), 76.73 (s), 62.29 (s), 61.69 (s), 56.67 (s). MS (ESI): 329.1 ($C_{18}H_{16}O$, $[M+H^+]$).

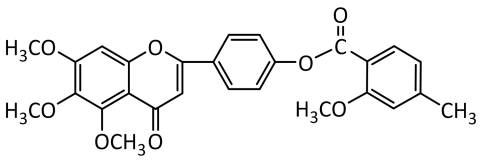
1.2 Synthesis of 2-(4-hydroxyphenyl)-5,6,7-trimethoxy-4H-chromen-4-one(4)



Reddish brown powder, yield: 81%. Mp:227-229 ℃. ^{1}H NMR (400 MHz, Acetone) δ 7.44 – 7.21 (m, 2H), 6.61 (s, 1H), 6.39 (s, 1H), 6.18 (s, 1H), 4.03 – 3.86 (m, 6H), 3.81 (s, 3H). ^{13}C NMR (101 MHz, Acetone) δ 180.65 (s), 167.60 (d, *J* = 3.0 Hz), 157.98 (s), 153.58 (s), 147.36 (s), 139.84 (s), 127.98 (s), 109.71 (s), 108.75 (s), 103.22 (s), 97.86 (s), 91.35 (s), 59.80 (s), 55.64 (s). MS (ESI): 344.1 ($C_{18}H_{16}O_7$, $[M+H^+]$).

1.3 Synthesis of compounds 7a-7g

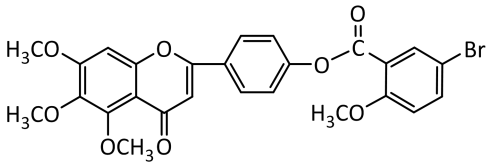
4-(5,6,7-trimethoxy-4-oxo-4H-chromen-2-yl)phenyl2-methoxy-4-methylbenzoate (7a)



Yellow powder, yield: 73%. Mp:199-200 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, *J* = 2.6 Hz, 1H), 7.91 (d, *J* = 8.7 Hz, 2H), 7.64 (dd, *J* = 8.9, 2.6 Hz, 1H), 7.28 (d, *J* = 8.7 Hz, 2H), 7.24 (s, 3H), 6.93 (d, *J* = 9.0 Hz, 1H), 6.76 (s, 1H), 6.55 (s, 1H), 4.25 (s, 3H), 3.98 (s, 3H), 3.92 (s, 3H), 3.81 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 180.79 (s), 164.06 (s), 162.66 (s), 161.74 (s), 159.10 (s), 151.75 (s), 151.40 (s), 147.63 (s), 137.14 (s), 136.68 (s), 134.72 (s), 132.35 (s), 130.36 (s),

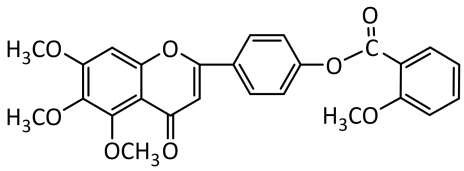
122.24 (s), 120.36 (s), 114.11 (s), 112.29 (s), 110.23 (s), 106.99 (s), 90.63 (s), 77.40 (s), 76.76 (s), 62.44 (s), 61.67 (s), 56.71 (s), 56.38 (s). MS (ESI): 477.1 ($C_{27}H_{24}O_8$, [M+H$^+$]).

4-(5,6,7-trimethoxy-4-oxo-4H-chromen-2-yl)phenyl5-bromo-2-methoxybenzoate (7b)



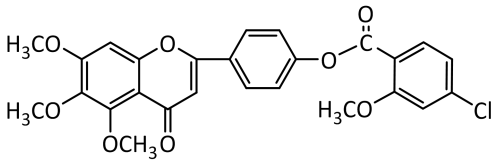
Yellow powder, yield: 85%. Mp:197-198 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, *J* = 2.6 Hz, 1H), 7.91 (d, *J* = 8.7 Hz, 2H), 7.64 (dd, *J* = 8.9, 2.5 Hz, 1H), 7.28 (d, *J* = 8.7 Hz, 2H), 6.93 (d, *J* = 8.9 Hz, 1H), 6.76 (s, 1H), 6.55 (s, 1H), 4.25 (s, 3H), 3.98 (s, 3H), 3.92 (s, 3H), 3.81 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 180.79 (s), 164.06 (s), 162.66 (s), 161.74 (s), 159.10 (s), 151.75 (s), 151.40 (s), 147.63 (s), 137.14 (s), 136.68 (s), 134.72 (s), 132.35 (s), 130.36 (s), 122.24 (s), 120.36 (s), 114.11 (s), 112.29 (s), 110.23 (s), 106.99 (s), 90.63 (s), 77.40 (s), 76.76 (s), 62.44 (s), 61.67 (s), 56.71 (s), 56.38 (s). MS (ESI): 542.0 ($C_{26}H_{21}O_8Br$, [M+H$^+$]).

4-(5,6,7-trimethoxy-4-oxo-4H-chromen-2-yl)phenyl2-methoxybenzoate (7c)



Light yellow powder, yield: 76%. Mp:174-176 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.91 (d, *J* = 8.7 Hz, 2H), 7.59 – 7.52 (m, 1H), 7.29 (d, *J* = 8.7 Hz, 2H), 7.05 (t, *J* = 7.5 Hz, 2H), 6.76 (s, 1H), 6.55 (s, 1H), 4.25 (s, 3H), 3.97 (s, 3H), 3.94 (s, 3H), 3.81 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 180.79 (s), 164.06 (s), 162.66 (s), 161.74 (s), 159.10 (s), 151.75 (s), 151.40 (s), 147.63 (s), 137.14 (s), 136.68 (s), 134.72 (s), 132.35 (s), 130.36 (s), 122.24 (s), 120.36 (s), 114.11 (s), 112.29 (s), 110.23 (s), 106.99 (s), 90.63 (s), 77.40 (s), 76.76 (s), 62.44 (s), 61.67 (s), 56.71 (s), 56.38 (s). MS (ESI): 463.1 ($C_{26}H_{22}O_8$, [M+H$^+$]).

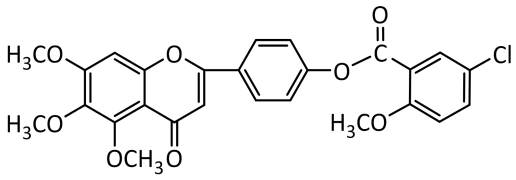
4-(5,6,7-trimethoxy-4-oxo-4H-chromen-2-yl)phenyl4-chloro-2-methoxybenzoate (7d)



Yellow powder, yield: 69%. Mp:144-151 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.7 Hz, 1H), 7.90 (d, *J* = 8.7 Hz, 2H), 7.27 (d, *J* = 8.7 Hz, 2H), 7.06 – 7.02 (m, 2H), 6.76 (s, 1H), 6.54 (s, 1H), 4.25 (s, 3H), 3.97 (s, 3H), 3.94 (s, 3H), 3.81 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 180.79 (s), 164.06 (s), 162.66 (s), 161.74 (s), 159.10 (s), 151.75 (s),

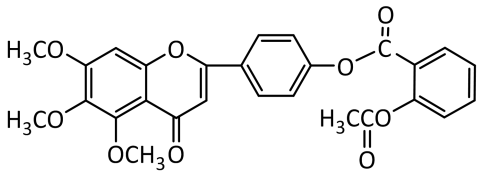
151.40 (s), 147.63 (s), 137.14 (s), 136.68 (s), 134.72 (s), 132.35 (s), 130.36 (s), 122.24 (s), 120.36 (s), 114.11 (s), 112.29 (s), 110.23 (s), 106.99 (s), 90.63 (s), 77.40 (s), 76.76 (s), 62.44 (s), 61.67 (s), 56.71 (s), 56.38 (s). MS (ESI): 498.1 ($C_{26}H_{21}O_8Cl$, [M+H$^+$]).

4-(5,6,7-trimethoxy-4-oxo-4H-chromen-2-yl)phenyl5-chloro-2-methoxybenzoate (7e)



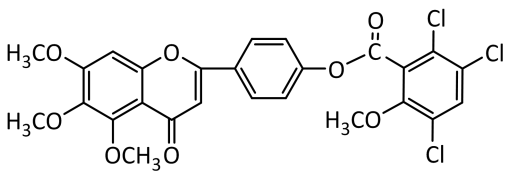
Yellow powder, yield: 71%. Mp:133-135 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (s, 1H), 7.83 (t, *J* = 12.9 Hz, 2H), 7.43 (t, *J* = 10.5 Hz, 1H), 7.20 (d, *J* = 7.3 Hz, 2H), 6.92 (d, *J* = 8.9 Hz, 1H), 6.72 (d, *J* = 20.0 Hz, 1H), 6.49 (s, 1H), 4.31 – 4.09 (m, 3H), 3.87 (t, *J* = 19.9 Hz, 6H), 3.72 (d, *J* = 27.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 180.82 (s), 164.07 (s), 162.80 (s), 161.76 (s), 158.62 (s), 151.76 (s), 151.42 (s), 147.64 (s), 134.20 (s), 132.35 (s), 131.85 (s), 130.36 (s), 125.34 (s), 122.22 (s), 119.97 (s), 113.72 (s), 110.26 (s), 90.64 (s), 77.31 (d, *J* = 11.6 Hz), 76.73 (s), 62.41 (s), 61.65 (s), 56.69 (s), 56.44 (s). MS (ESI):498.1($C_{26}H_{21}O_8Cl$, [M+H$^+$]).

4-(5,6,7-trimethoxy-4-oxo-4H-chromen-2-yl)phenyl 2-acetoxybenzoate (7f)



Light yellow powder, yield: 66%. Mp:166-169 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (t, *J* = 11.6 Hz, 1H), 7.86 (d, *J* = 8.4 Hz, 2H), 7.59 (t, *J* = 7.7 Hz, 1H), 7.36 (dt, *J* = 15.3, 7.5 Hz, 1H), 7.19 (d, *J* = 1.4 Hz, 2H), 7.12 (d, *J* = 8.1 Hz, 1H), 6.70 (s, 1H), 6.48 (s, 1H), 4.16 (d, *J* = 22.8 Hz, 3H), 3.89 (d, *J* = 18.8 Hz, 3H), 3.79 (d, *J* = 29.7 Hz, 3H), 2.25 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 180.80 (s), 169.78 (s), 164.08 (s), 162.70 (s), 161.78 (s), 151.78 (s), 151.22 (d, *J* = 12.4 Hz), 147.71 (s), 136.71 (s), 134.86 (s), 132.46 (s), 132.26 (s), 130.60 (s), 126.29 (s), 124.12 (s), 122.26 (d, *J* = 5.1 Hz), 110.09 (s), 106.98 (s), 90.62 (s), 77.39 (s), 76.75 (s), 62.44 (s), 61.66 (s), 56.71 (s), 21.06 (s). MS (ESI):491.1 ($C_{27}H_{22}O_9$, [M+H$^+$]).

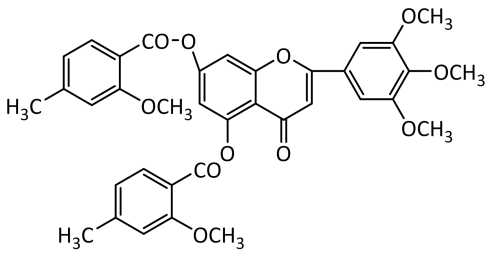
4-(5,6,7-trimethoxy-4-oxo-4H-chromen-2-yl)phenyl 2,3,5-trichloro-6-methoxybenzoate (7g)



Yellow-green powder, yield:58%. Mp:196-198 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 8.7 Hz, 2H), 7.61 (s, 1H), 7.33 (d, *J* = 8.7 Hz, 2H), 6.76 (s, 1H), 6.53 (s, 1H), 4.25 (s, 3H), 3.98 (d, *J* = 3.3 Hz, 6H), 3.81 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 180.74 (s), 164.08 (s), 162.17 (s), 161.82 (s), 150.79 (s), 132.49 (s), 131.12 (s), 129.23 (s), 127.47 (s), 121.85 (s), 109.78 (s), 90.58 (s), 77.38 (s), 76.74 (s), 62.64 (s), 62.42 (s), 61.65 (s), 56.70 (s). MS (ESI): 565.9 ($C_{26}H_{19}O_8Cl_3$,[M+H$^+$]).

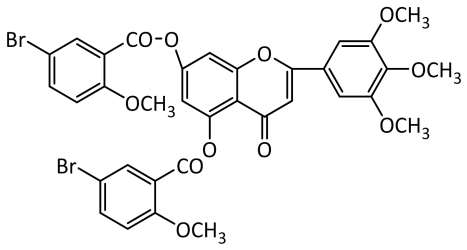
1.4 Synthesis of compounds 8a-8g

4-oxo-2-(3,4,5-trimethoxyphenyl)-4H-chromene-5,7-diyl bis(2-methoxy-4-methylbenzoate) (8a)



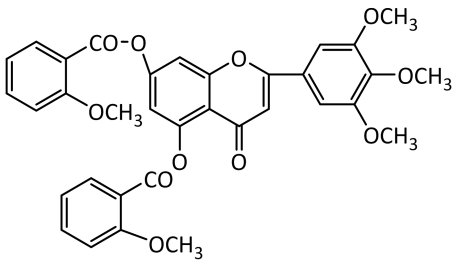
Yellow powder, yield: 75%. Mp:111-115 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 – 8.13 (m, 1H), 7.92 (t, *J* = 6.7 Hz, 1H), 7.23 (dd, *J* = 7.7, 1.4 Hz, 2H), 7.03 (t, *J* = 5.0 Hz, 1H), 6.96 – 6.80 (m, 5H), 6.70 (s, 1H), 3.94 – 3.87 (m, 15H), 2.42 (s, 6H).^{13}C NMR (101 MHz, $CDCl_3$) δ 180.48 (s), 166.35 (s), 162.68 (s), 162.33 (s), 160.62 (s), 158.29 (s), 153.32 (s), 148.80 (s), 146.70 (d, *J* = 5.5 Hz), 146.22 (s), 140.02 (s), 133.12 (s), 132.59 (s), 127.57 (s), 121.27 (d, *J* = 7.5 Hz), 114.77 (d, *J* = 23.6 Hz), 113.26 – 112.76 (m), 112.20 (s), 111.52 (s), 108.80 (s), 104.16 (s), 77.40 (s), 76.77 (s), 61.03 (s), 56.11 (d, *J* = 18.1 Hz), 22.17 (s). MS (ESI):641.4 ($C_{36}H_{32}O_{11}$, [M+H$^+$]).

4-oxo-2-(3,4,5-trimethoxyphenyl)-4H-chromene-5,7-diyl bis(5-bromo-2-methoxybenzoate) (8b)



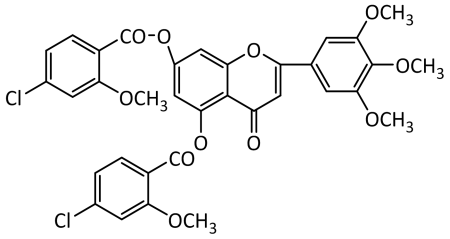
Orange powder, yield: 54%. Mp:199-202 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, *J* = 2.6 Hz, 1H), 8.11 (d, *J* = 2.6 Hz, 1H), 7.69 – 7.63 (m, 2H), 7.12 (s, 2H), 7.02 – 6.89 (m, 4H), 6.75 (s, 1H), 3.92 (dd, *J* = 8.5, 6.1 Hz, 15H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 180.27 (s), 166.26 (s), 161.55 (s), 161.21 (s), 159.38 (s), 157.74 (s), 153.34 (s), 148.26 (s), 146.54 (s), 140.20 (s), 137.71 (s), 137.41 (s), 135.37 (s), 134.83 (s), 127.38 (s), 119.58 (s), 119.38 (s), 114.12 (d, *J* = 14.3 Hz), 113.71 (s), 112.39 (d, *J* = 9.3 Hz), 111.25 (s), 108.91 (s), 104.45 (s), 77.39 (s), 76.76 (s), 61.05 (s), 56.31 (d, *J* = 19.5 Hz). MS (ESI): 770.8 ($C_{34}H_{26}O_{11}Br_2$, [M+H$^+$]).

4-oxo-2-(3,4,5-trimethoxyphenyl)-4H-chromene-5,7-diyl bis(2-methoxybenzoate) (8c)



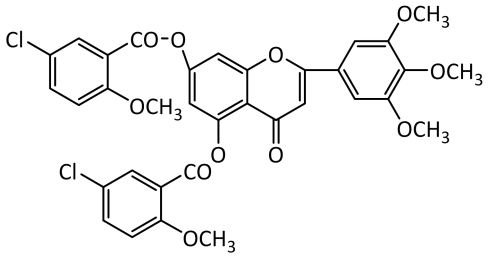
Yellowish brown powder, yield: 62%. Mp:195-198 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (d, *J* = 7.9 Hz, 1H), 8.02 (d, *J* = 6.5 Hz, 1H), 7.58 (dd, *J* = 15.0, 7.9 Hz, 2H), 7.20 – 6.96 (m, 8H), 6.72 (s, 1H), 3.93 (dd, *J* = 15.3, 6.2 Hz, 15H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 180.44 (s), 166.35 (s), 162.86 (s), 162.47 (s), 160.35 (s), 158.16 (s), 153.34 (s), 148.67 (s), 146.68 (s), 140.11 (s), 135.19 (s), 134.85 (s), 133.02 (s), 132.47 (s), 127.50 (s), 120.38 (d, *J* = 8.6 Hz), 117.94 (s), 117.72 (s), 113.30 (s), 112.23 (d, *J* = 14.9 Hz), 111.49 (s), 108.85 (s), 104.30 (s), 77.39 (s), 76.76 (s), 61.04 (s), 56.15 (d, *J* = 12.2 Hz). MS (ESI): 611.7($C_{34}H_{28}O_{11}$,[M+H$^+$]).

4-oxo-2-(3,4,5-trimethoxyphenyl)-4H-chromene-5,7-diyl bis(4-chloro-2-methoxybenzoate) (8d)



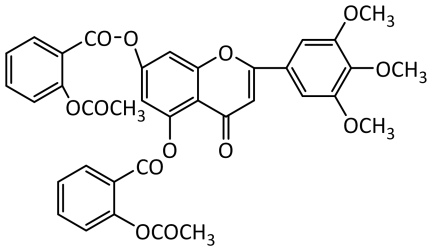
Yellow powder, yield: 59%. Mp:224-227 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, *J* = 8.3 Hz, 1H), 7.99 (d, *J* = 7.8 Hz, 1H), 7.25 (d, *J* = 9.4 Hz, 2H), 7.15 – 7.02 (m, 6H), 6.74 (s, 1H), 3.95 (dd, *J* = 13.4, 5.0 Hz, 15H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 180.40 (s), 166.30 (s), 162.04 (s), 161.65 (s), 160.95 (s), 157.89 (s), 153.34 (s), 148.43 (s), 146.59 (s), 141.35 (s), 140.94 (s), 140.18 (s), 134.11 (s), 133.56 (s), 127.39 (s), 120.76 (d, *J* = 4.6 Hz), 116.33 (s), 116.09 (s), 113.60 (s), 112.97 (d, *J* = 18.3 Hz), 112.33 (s), 111.36 (s), 108.88 (s), 104.38 (s), 77.39 (s), 76.75 (s), 61.06 (s), 56.52 – 56.11 (m). MS (ESI): 682.1 ($C_{34}H_{26}O_{11}Cl_2$, [M+H$^+$]).

4-oxo-2-(3,4,5-trimethoxyphenyl)-4H-chromene-5,7-diyl bis(5-chloro-2-methoxybenzoate) (8e)



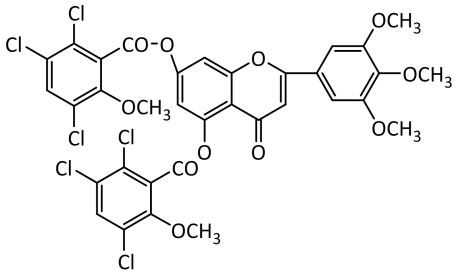
Yellow powder, yield: 52%. Mp:115-116 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (s, 1H), 8.00 (s, 1H), 7.55 (dd, *J* = 8.2, 5.9 Hz, 2H), 7.32 – 6.96 (m, 6H), 6.77 (s, 1H), 4.31 – 3.57 (m, 15H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 180.32 (s), 166.27 (s), 161.68 (s), 161.35 (s), 158.90 (d, *J* = 2.8 Hz), 157.75 (s), 153.33 (s), 148.26 (s), 146.54 (s), 140.17 (s), 134.83 (s), 134.52 (s), 132.51 (s), 131.97 (s), 127.38 (s), 125.42 (d, *J* = 3.8 Hz), 119.10 (s), 118.88 (s), 113.92 – 113.53 (m), 112.45 (s), 111.27 (s), 108.89 (s), 104.47 (s), 77.40 (s), 76.76 (s), 61.06 (s), 56.46 (s), 56.21 (s). MS (ESI): 682.1 ($C_{34}H_{26}O_{11}Cl_2$, [M+H$^+$]).

4-oxo-2-(3,4,5-trimethoxyphenyl)-4H-chromene-5,7-diyl bis(2-acetoxybenzoate) (8f)



yellowish brown, yield: 59%. Mp:168-170 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (dd, *J* = 7.9, 1.6 Hz, 1H), 8.21 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.67 (dt, *J* = 9.6, 4.6 Hz, 2H), 7.42 (td, *J* = 6.8, 3.8 Hz, 2H), 7.22 – 7.15 (m, 3H), 7.11 (s, 2H), 6.97 (d, *J* = 1.7 Hz, 1H), 6.75 (s, 1H), 3.91 (d, *J* = 6.2 Hz, 9H), 2.32 (d, *J* = 10.7 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 180.11 (s), 169.68 (d, *J* = 10.2 Hz), 166.27 (s), 161.67 (s), 161.28 (s), 157.51 (s), 153.36 (s), 151.49 (s), 148.20 (s), 146.42 (s), 140.29 (s), 135.42 (s), 135.01 (s), 132.69 (s), 132.23 (s), 127.28 (s), 126.40 (d, *J* = 3.5 Hz), 124.17 (d, *J* = 21.6 Hz), 124.02 – 123.83 (m), 121.61 (d, *J* = 18.0 Hz), 113.95 (s), 112.61 (s), 111.31 (s), 108.96 (s), 104.77 (s), 77.42 (s), 76.78 (s), 61.06 (s), 56.25 (s), 21.06 (s). MS (ESI): 668.8 ($C_{36}H_{28}O_{13}$, [M+H$^+$]).

4-oxo-2-(3,4,5-trimethoxyphenyl)-4H-chromene-5,7-diyl bis(2,3,5-trichloro-6-methoxybenzoate) (8g)

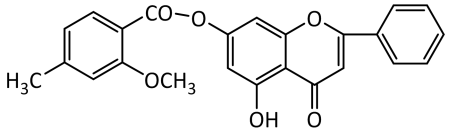


Orange powder, yield: 42%. Mp:214-219 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, *J* = 3.3 Hz, 2H), 7.24 (s, 1H), 7.08 (s, 2H), 6.99 (s, 1H), 6.75 (s, 1H), 4.00 (s, 3H), 3.93 (s, 3H), 3.86 (d, *J* = 11.0 Hz, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 179.66 (s), 166.32 (s), 161.16 (s), 160.67 (s), 156.76 (s), 153.21 (d, *J* = 14.9 Hz), 152.64 (s), 147.26 (s), 146.14 (s), 140.38 (s), 132.90 (d, *J* = 5.9 Hz), 129.83 (s), 129.63 (s), 129.26 (d, *J* = 12.3 Hz), 128.80 (s), 128.24 (s), 127.55 (d, *J* =

7.5 Hz), 127.13 (s), 114.50 (s), 113.18 (s), 110.62 (s), 109.15 (s), 104.98 (s), 77.44 (s), 76.81 (s), 62.75 (d, *J* = 15.1 Hz), 60.97 (s), 56.24 (s), 50.12 (s). MS (ESI): 820.1 ($C_{34}H_{22}O_{11}Cl_6$, [M+H$^+$]).

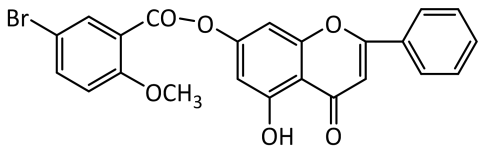
1.5 Synthesis of compounds 9a-9g

5-hydroxy-4-oxo-2-phenyl-4H-chromen-7-yl 2-methoxy-4-methylbenzoate (9a)



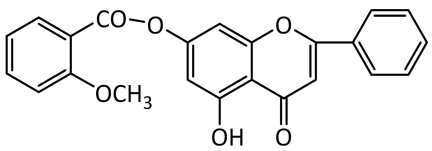
Light yellow powder, yield: 67%. Mp:172-173 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.71 (s, 1H), 7.95 – 7.85 (m, 3H), 7.58 – 7.49 (m, 3H), 7.00 (d, *J* = 2.0 Hz, 1H), 6.88 – 6.83 (m, 2H), 6.73 (s, 1H), 6.68 (d, *J* = 2.0 Hz, 1H), 3.93 (s, 3H), 2.43 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.95 (s), 164.63 (s), 163.05 (s), 161.82 (s), 160.45 (s), 156.68 (d, *J* = 19.9 Hz), 146.37 (s), 132.54 (s), 132.12 (s), 131.05 (s), 129.18 (s), 126.40 (s), 121.19 (s), 115.09 (s), 113.00 (s), 108.79 (s), 106.09 (s), 105.78 (s), 101.43 (s), 77.38 (s), 76.75 (s), 56.02 (s), 22.16 (s). MS (ESI): 387.1 ($C_{24}H_{18}O_5$, [M+H$^+$]).

5-hydroxy-4-oxo-2-phenyl-4H-chromen-7-yl 5-bromo-2-methoxybenzoate (9b)



Light yellow powder, yield: 76%. Mp:198-199 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.76 (s, 1H), 8.12 (s, 1H), 7.91 (d, *J* = 6.9 Hz, 2H), 7.68 (d, *J* = 8.9 Hz, 1H), 7.55 (d, *J* = 8.1 Hz, 3H), 7.04 – 6.92 (m, 2H), 6.76 (s, 1H), 6.71 (s, 1H), 3.95 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.93 (s), 164.73 (s), 161.94 (s), 159.20 (s), 156.78 (s), 156.05 (s), 137.44 (s), 134.77 (s), 132.20 (s), 130.97 (s), 129.21 (s), 126.43 (s), 119.87 (s), 114.14 (s), 112.33 (s), 109.01 (s), 106.16 (s), 105.66 (s), 101.26 (s), 77.38 (s), 76.75 (s), 56.40 (s). MS (ESI): 451.9 ($C_{23}H_{15}O_5Br$, [M+H$^+$]).

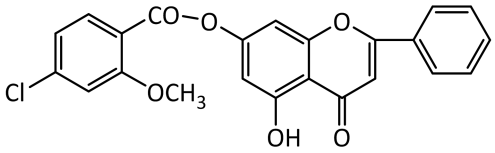
5-hydroxy-4-oxo-2-phenyl-4H-chromen-7-yl 2-methoxybenzoate (9c)



Yellow and white powder, yield: 74%. Mp:162-163 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.72 (s, 1H), 8.01 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.89 (dd, *J* = 8.0, 1.6 Hz, 2H), 7.60 – 7.49 (m, 4H), 7.06 (t, *J* = 7.6 Hz, 2H), 7.01 (d, *J* = 2.0 Hz, 1H), 6.74 (s, 1H), 6.69 (d, *J* = 2.0 Hz, 1H), 3.95 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.90 (s), 164.61 (s), 163.22 (s), 161.84 (s), 160.16 (s), 156.75 (s), 156.43 (s), 134.93 (s), 132.37 (s), 132.15 (s), 130.95 (s), 129.17 (s), 126.37 (s), 120.30 (s),

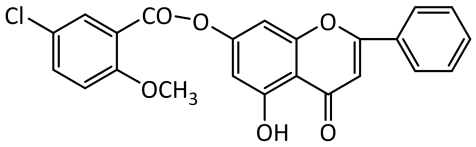
118.15 (s), 112.28 (s), 108.84 (s), 106.05 (s), 105.72 (s), 101.37 (s), 77.43 (s), 76.80 (s), 56.08 (s). MS (ESI): 373.1 ($C_{23}H_{16}O_5$, [M+H$^+$]).

5-hydroxy-4-oxo-2-phenyl-4H-chromen-7-yl 4-chloro-2-methoxybenzoate (9d)



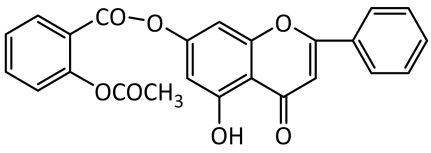
Light yellow powder, yield: 80%. Mp:194-195 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.77 (s, 1H), 8.21 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.89 (dd, *J* = 8.1, 1.6 Hz, 2H), 7.70 – 7.64 (m, 1H), 7.54 (dd, *J* = 6.9, 4.6 Hz, 2H), 7.41 (td, *J* = 7.8, 1.1 Hz, 1H), 7.20 – 7.17 (m, 1H), 6.93 (d, *J* = 2.1 Hz, 1H), 6.74 (s, 1H), 6.66 (d, *J* = 2.1 Hz, 1H), 2.32 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.89 (s), 164.66 (s), 162.39 (s), 161.89 (s), 160.77 (s), 156.76 (s), 156.18 (s), 140.99 (s), 133.48 (s), 132.17 (s), 130.96 (s), 129.18 (s), 126.39 (s), 120.66 (s), 116.60 (s), 113.00 (s), 108.92 (s), 106.11 (s), 105.64 (s), 101.28 (s), 77.39 (s), 76.75 (s), 56.39 (s). MS (ESI): 407.4 ($C_{23}H_{15}O_5Cl$, [M+H$^+$]).

5-hydroxy-4-oxo-2-phenyl-4H-chromen-7-yl 5-chloro-2-methoxybenzoate (9e)



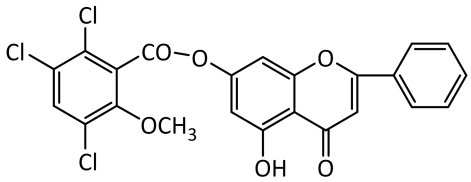
Light yellow powder, yield: 78%. Mp:198-198.5 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.74 (s, 1H), 7.97 (d, *J* = 2.7 Hz, 1H), 7.91 – 7.87 (m, 2H), 7.57 – 7.49 (m, 4H), 6.99 (dd, *J* = 5.5, 3.5 Hz, 2H), 6.74 (s, 1H), 6.69 (d, *J* = 2.0 Hz, 1H), 3.94 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.91 (s), 164.72 (s), 162.01 (d, *J* = 14.5 Hz), 158.72 (s), 156.79 (s), 156.07 (s), 134.50 (s), 132.18 (s), 131.89 (s), 130.98 (s), 129.20 (s), 126.42 (s), 125.39 (s), 113.73 (s), 109.00 (s), 106.15 (s), 105.64 (s), 101.24 (s), 77.36 (s), 76.73 (s), 56.45 (s). MS (ESI):507.4 ($C_{23}H_{15}O_5Cl$, [M+H$^+$]).

5-hydroxy-4-oxo-2-phenyl-4H-chromen-7-yl 2-acetoxybenzoate (9f)



White powder, yield: 71%. Mp:191-192 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.79 (s, 1H), 8.23 (d, *J* = 7.8 Hz, 1H), 7.91 (d, *J* = 7.0 Hz, 2H), 7.69 (t, *J* = 7.7 Hz, 1H), 7.56 (d, *J* = 7.8 Hz, 3H), 7.43 (t, *J* = 7.7 Hz, 1H), 7.21 (d, *J* = 8.1 Hz, 1H), 6.95 (s, 1H), 6.77 (s, 1H), 6.68 (s, 1H), 2.34 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.91 (s), 169.73 (s), 164.79 (s), 162.02 (d, *J* = 9.0 Hz), 156.83 (s), 155.84 (s), 151.40 (s), 135.16 (s), 132.26 (s), 130.90 (s), 129.22 (s), 126.40 (d, *J* = 10.4 Hz), 124.20 (s), 121.86 (s), 109.15 (s), 106.16 (s), 105.69 (s), 101.28 (s), 77.38 (s), 76.75 (s), 21.06 (s). MS (ESI): 401.1 ($C_{24}H_{16}O_6$, [M+H$^+$]).

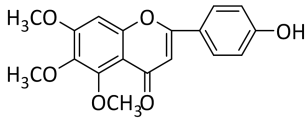
5-hydroxy-4-oxo-2-phenyl-4H-chromen-7-yl 2,3,5-trichloro-6-methoxybenzoate (9g)

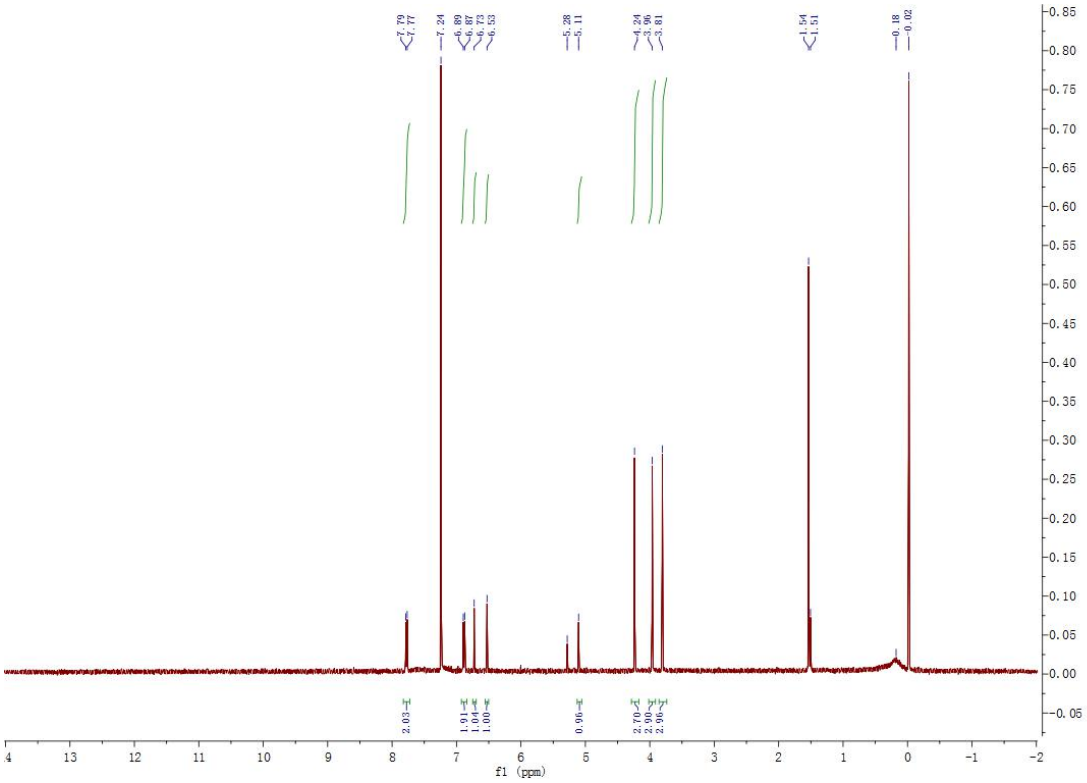


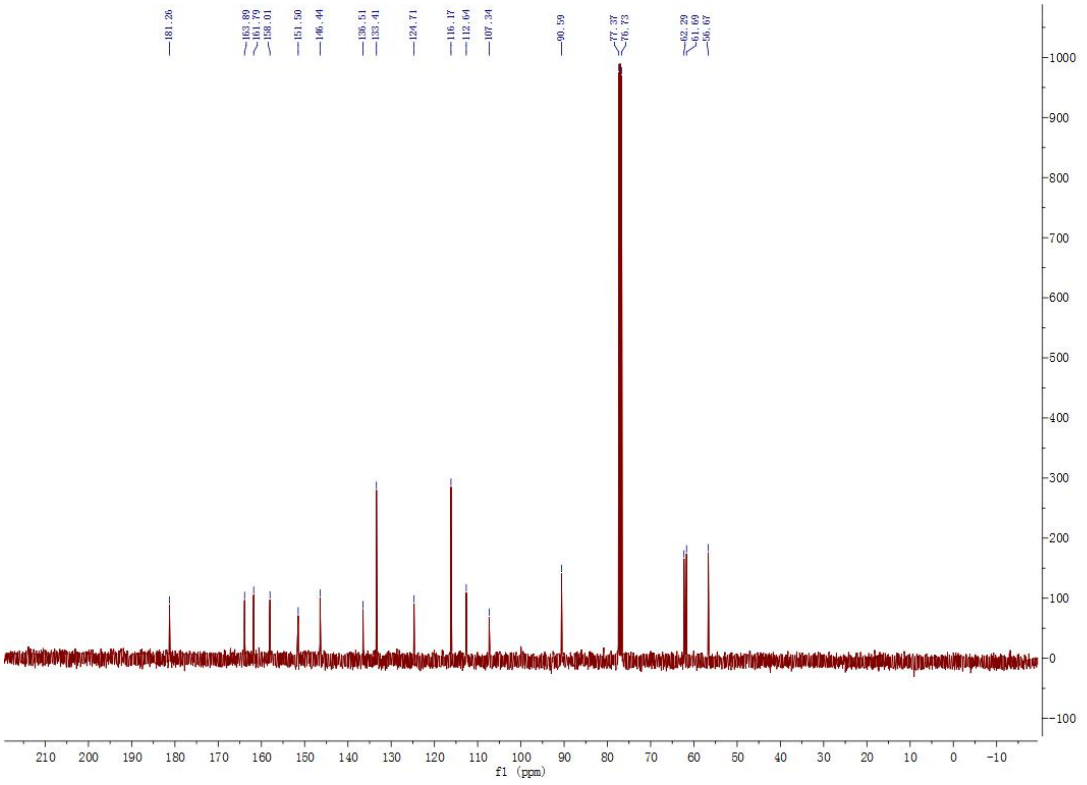
Light yellow powder, yield: 67%. Mp:173-173 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.82 (s, 1H), 7.93 – 7.89 (m, 2H), 7.63 (s, 1H), 7.59 – 7.51 (m, 3H), 7.00 (d, *J* = 2.1 Hz, 1H), 6.76 (s, 1H), 6.73 (d, *J* = 2.0 Hz, 1H), 4.00 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.85 (s), 164.89 (s), 162.17 (s), 161.46 (s), 156.85 (s), 155.27 (s), 132.68 (s), 132.31 (s), 130.81 (s), 130.32 (s), 129.22 (s), 127.49 (s), 126.47 (s), 109.43 (s), 106.23 (s), 105.37 (s), 100.93 (s), 77.37 (s), 76.73 (s), 62.67 (s). MS (ESI): 476.6 ($C_{23}H_{13}O_5Cl_3$, [M+H^+]).

2. ^{1}H NMR and ^{13}C NMR spectra

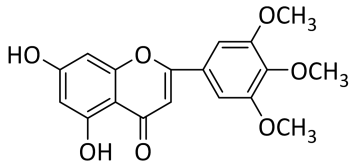
5,7-dihydroxy-2-(3,4,5-trimethoxyphenyl)-4H-chromen-4-one (2)

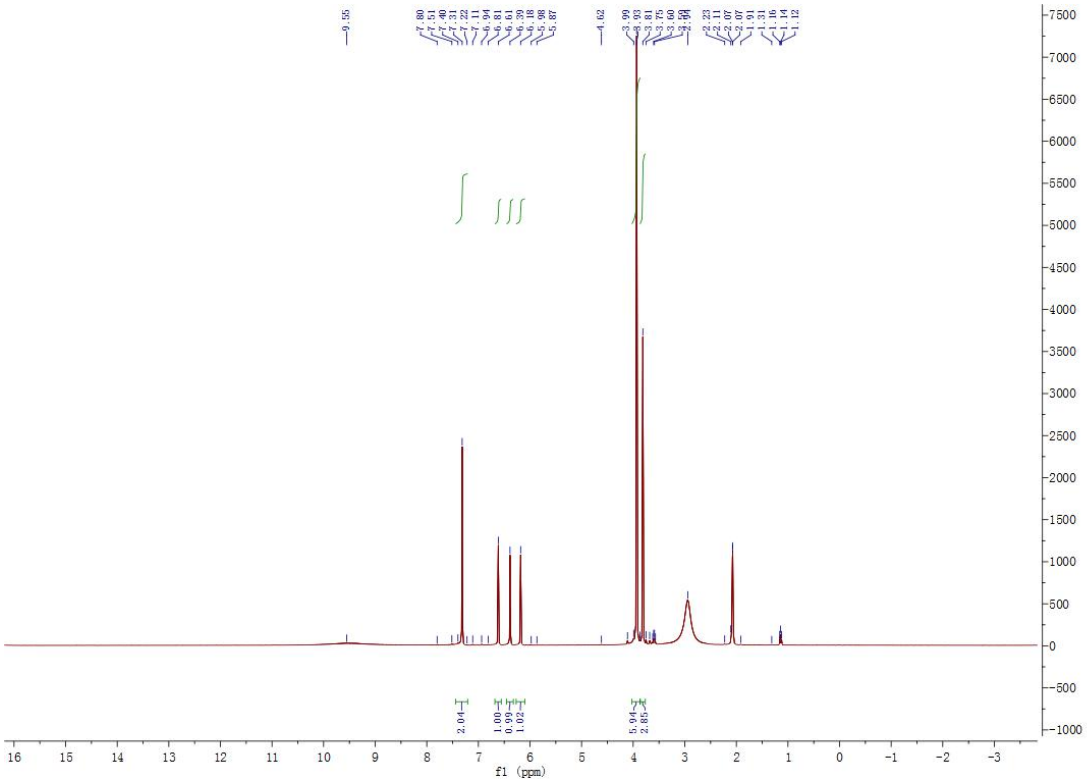


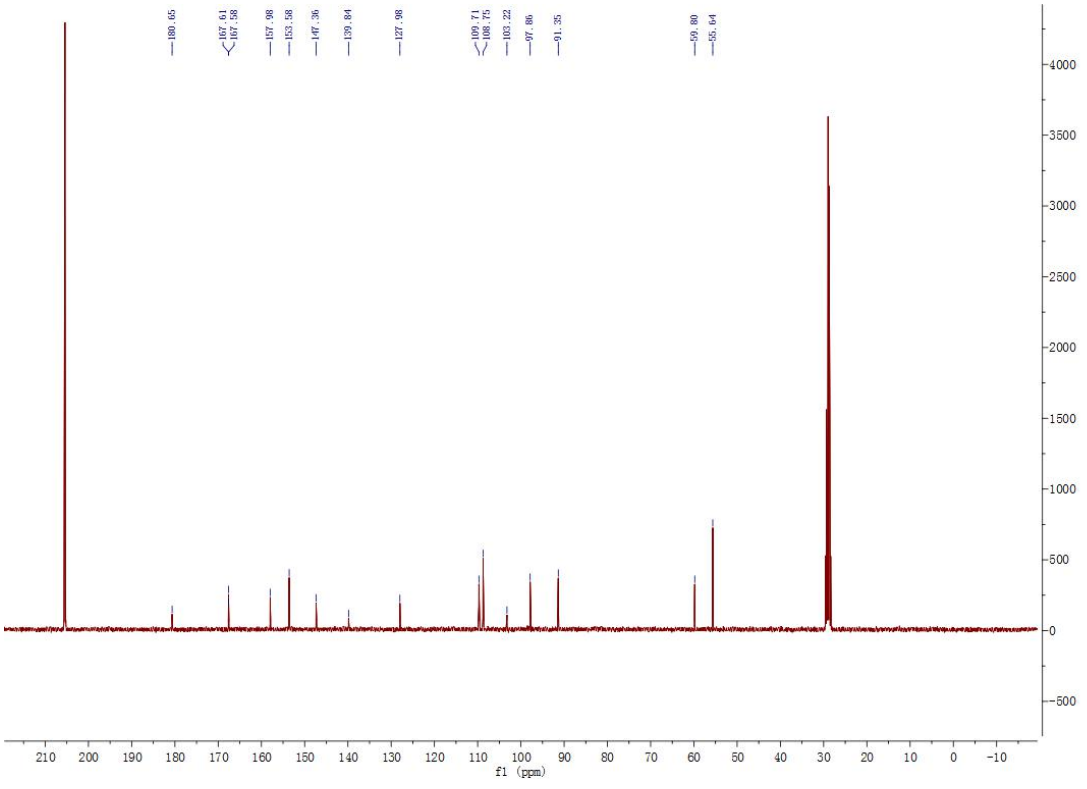




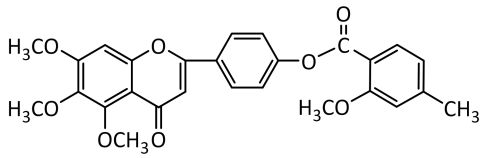
2-(4-hydroxyphenyl)-5,6,7-trimethoxy-4H-chromen-4-one(4)

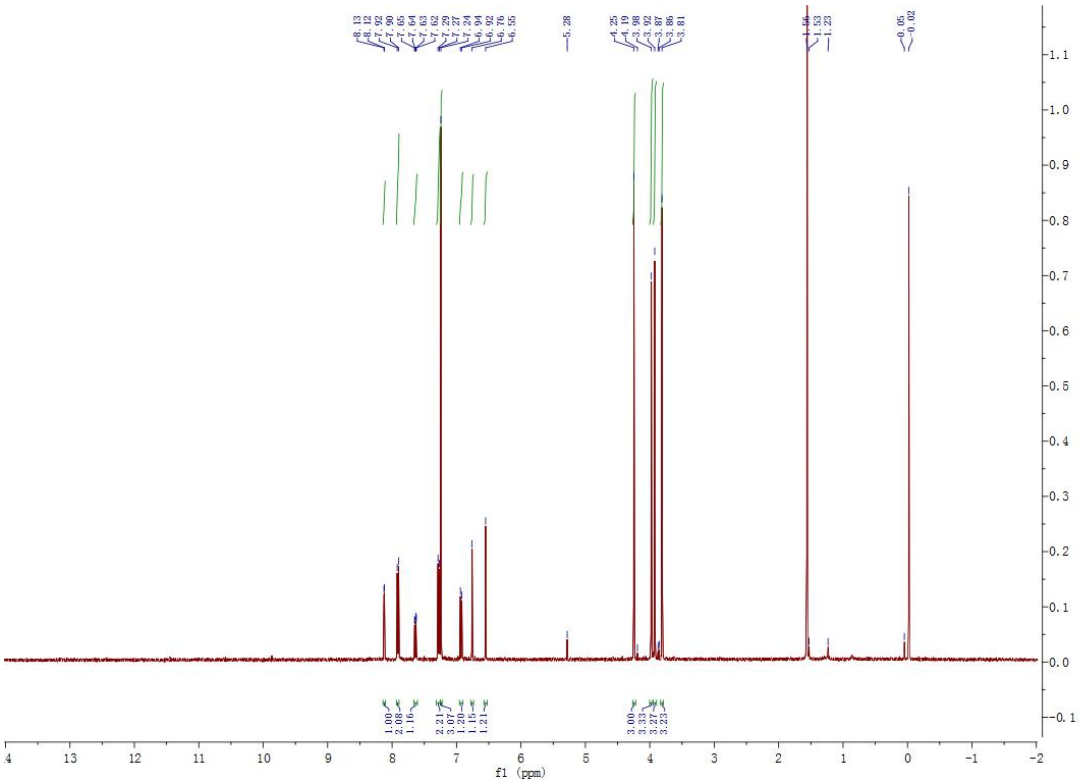


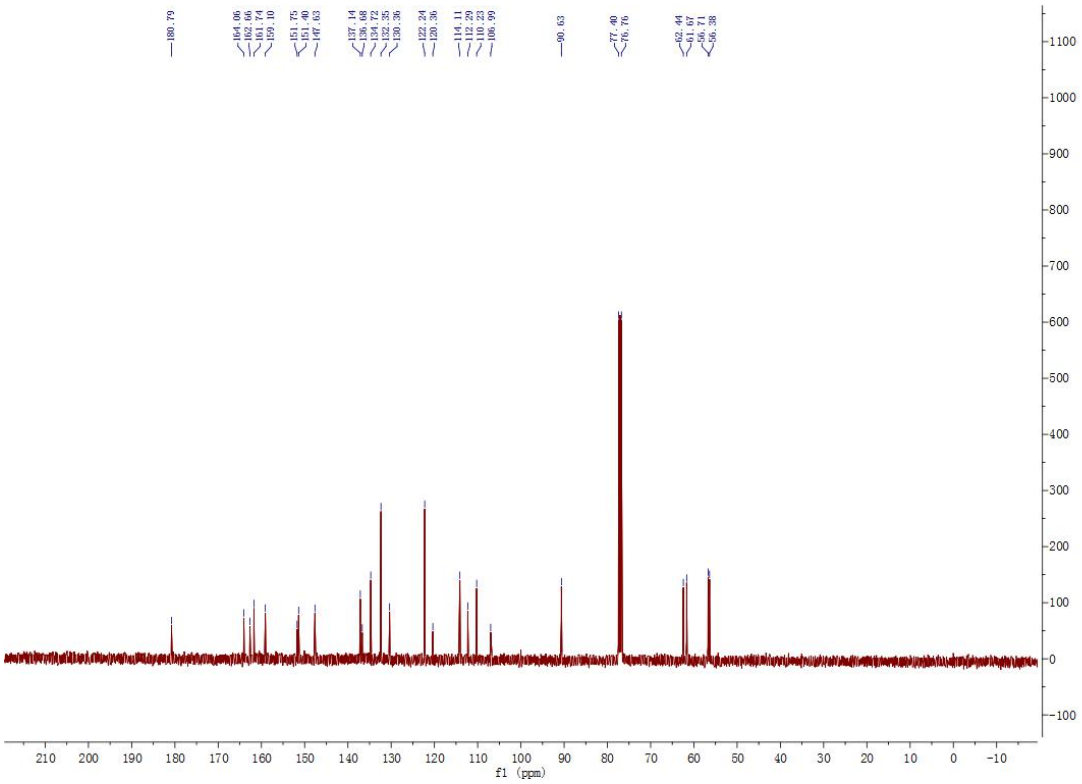




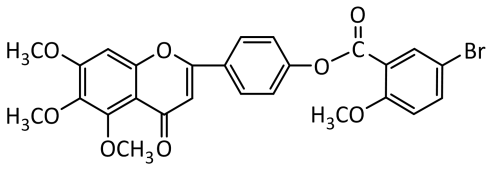
4-(5,6,7-trimethoxy-4-oxo-4H-chromen-2-yl)phenyl2-methoxy-4-methylbenzoate (7a)

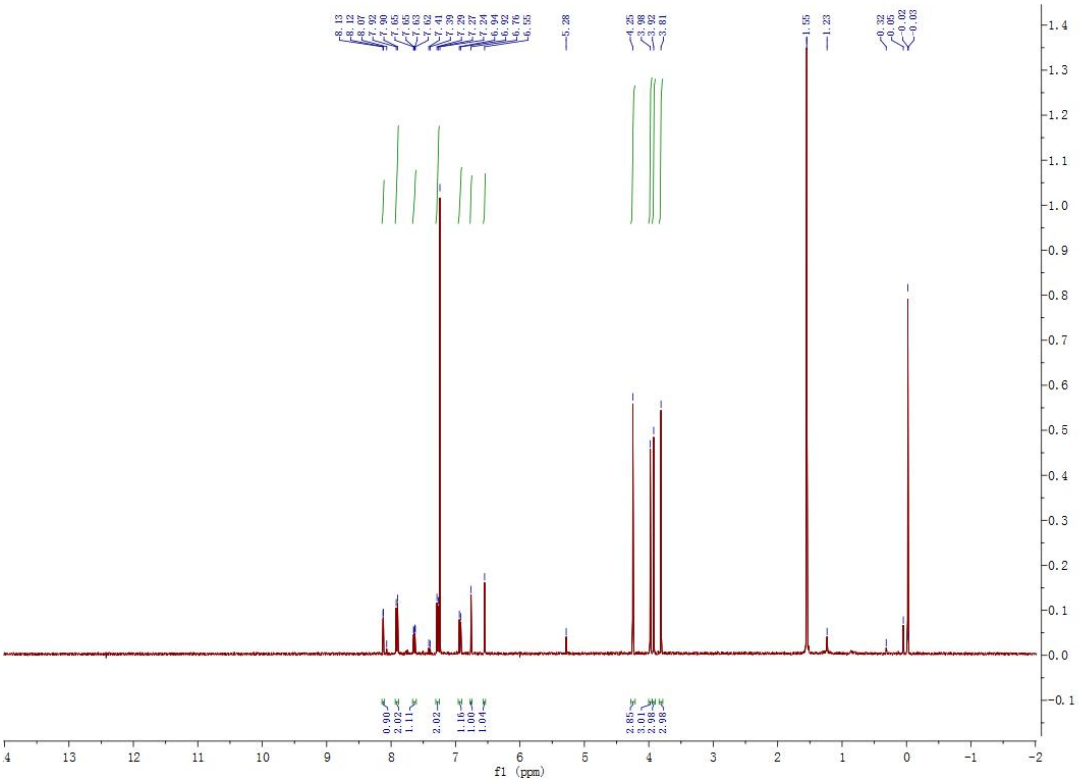


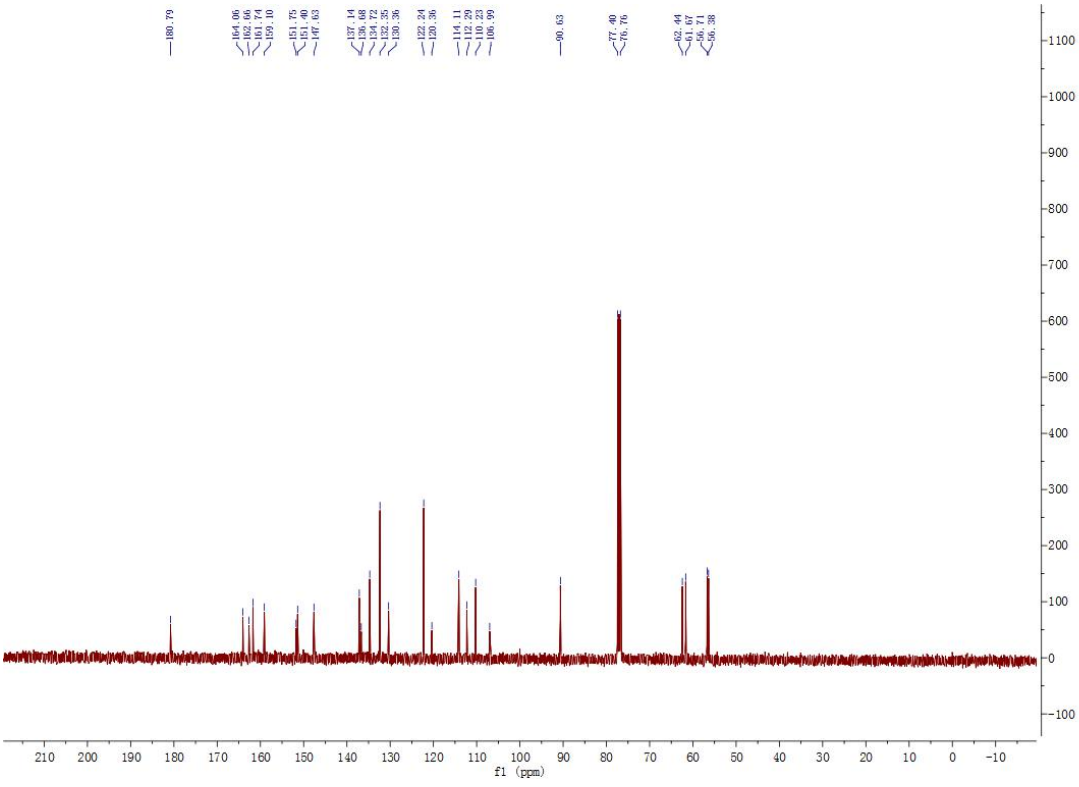




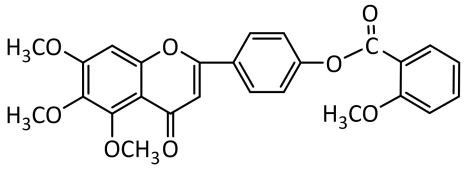
4-(5,6,7-trimethoxy-4-oxo-4H-chromen-2-yl)phenyl5-bromo-2-methoxybenzoate (7b)

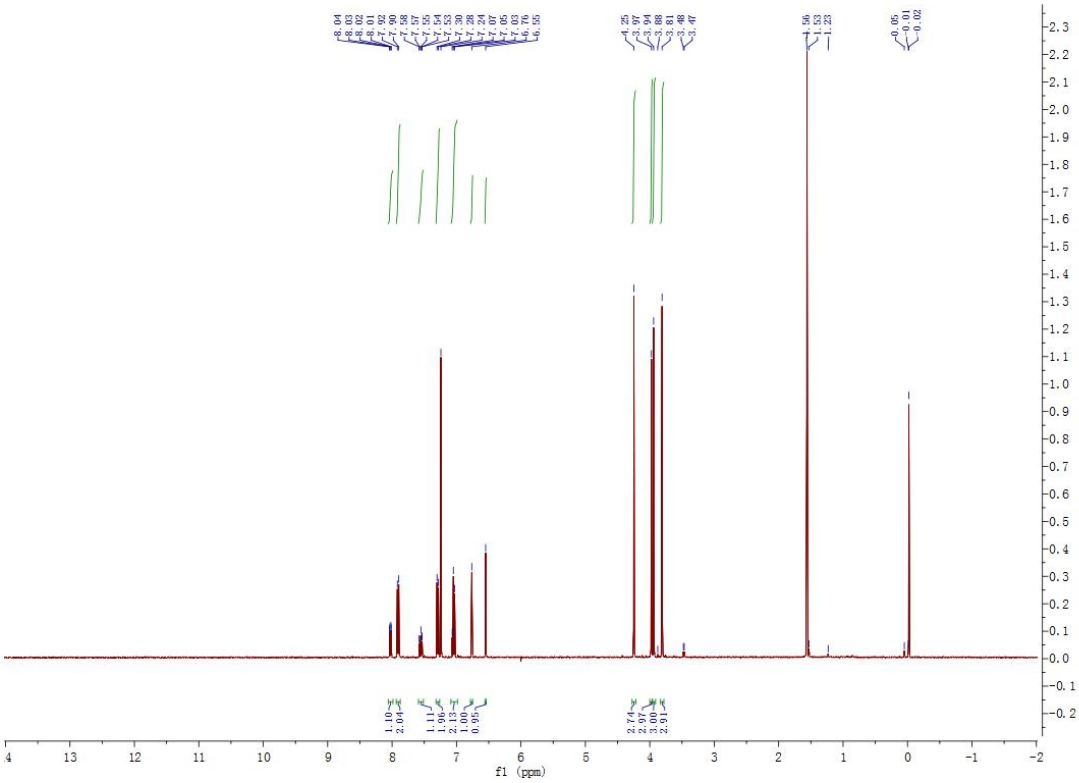


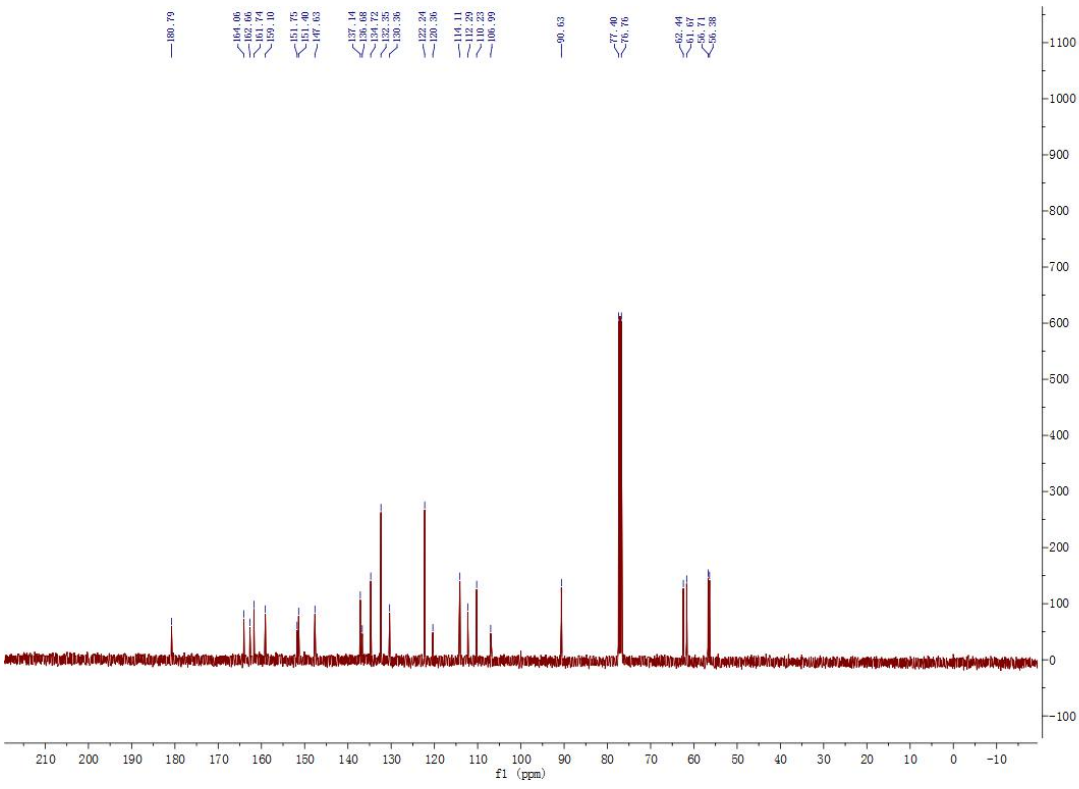




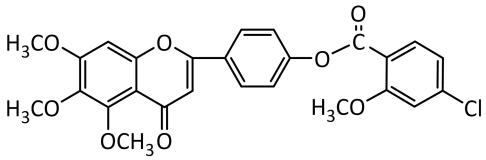
4-(5,6,7-trimethoxy-4-oxo-4H-chromen-2-yl)phenyl2-methoxybenzoate (7c)

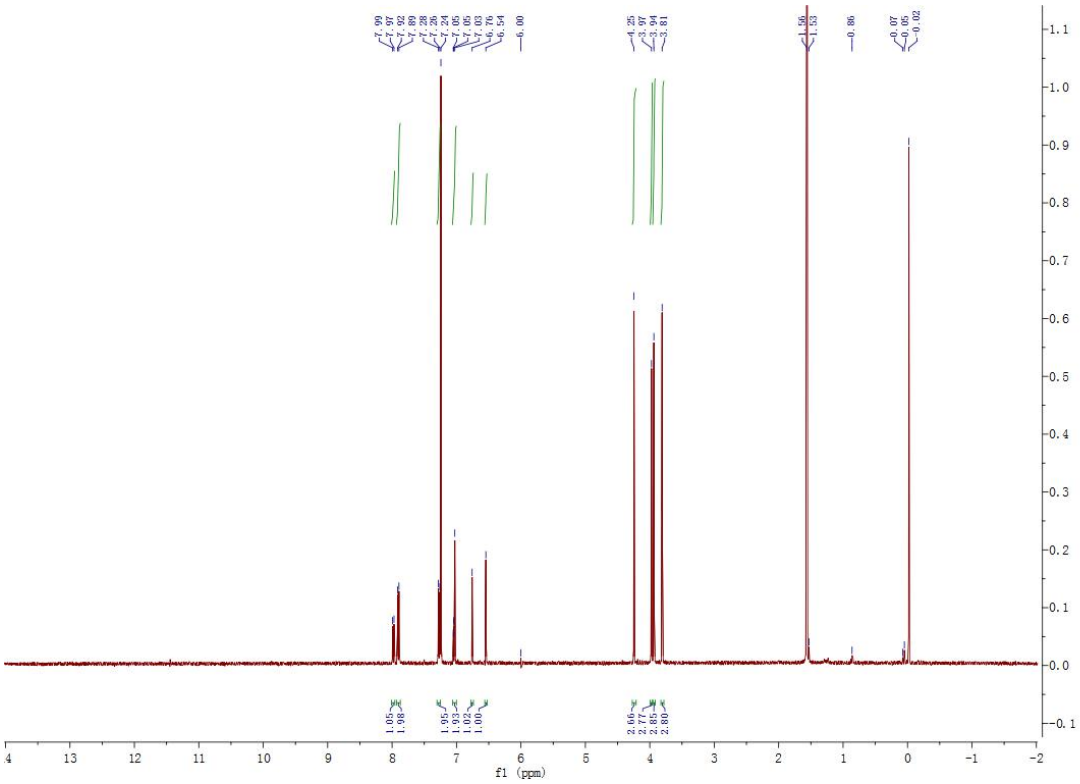


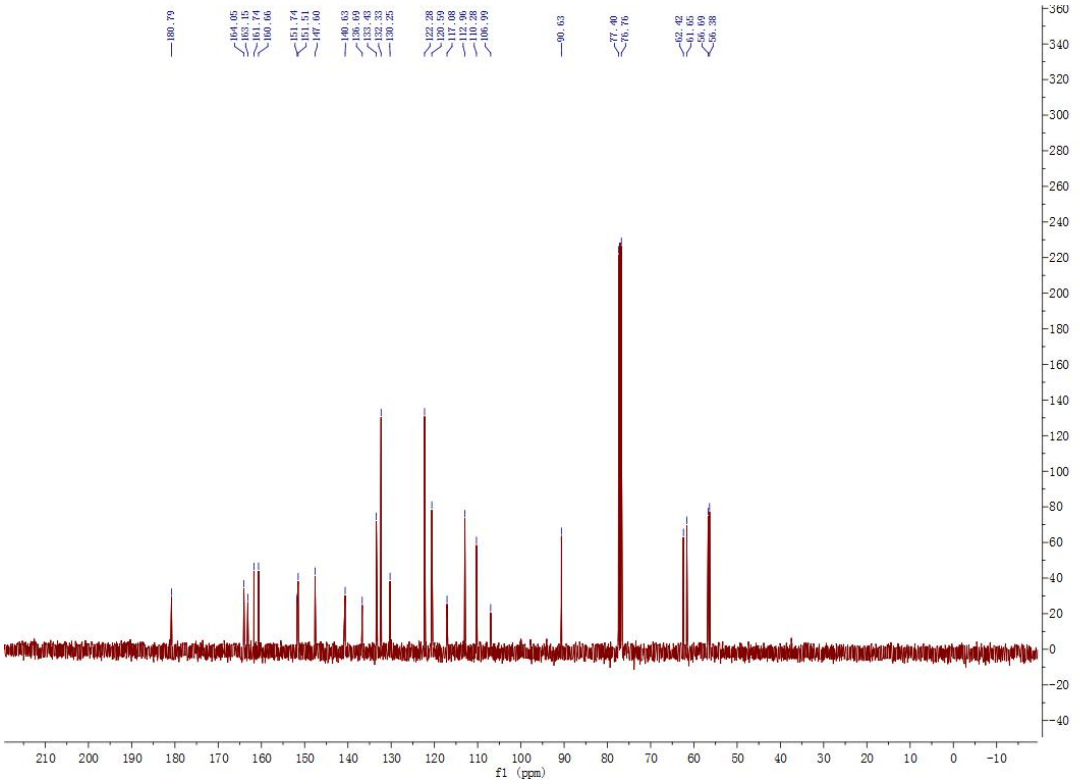




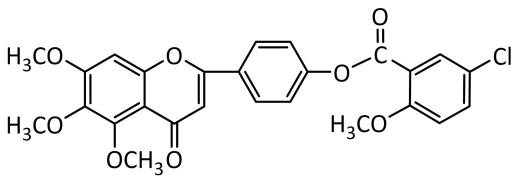
4-(5,6,7-trimethoxy-4-oxo-4H-chromen-2-yl)phenyl4-chloro-2-methoxybenzoate (7d)

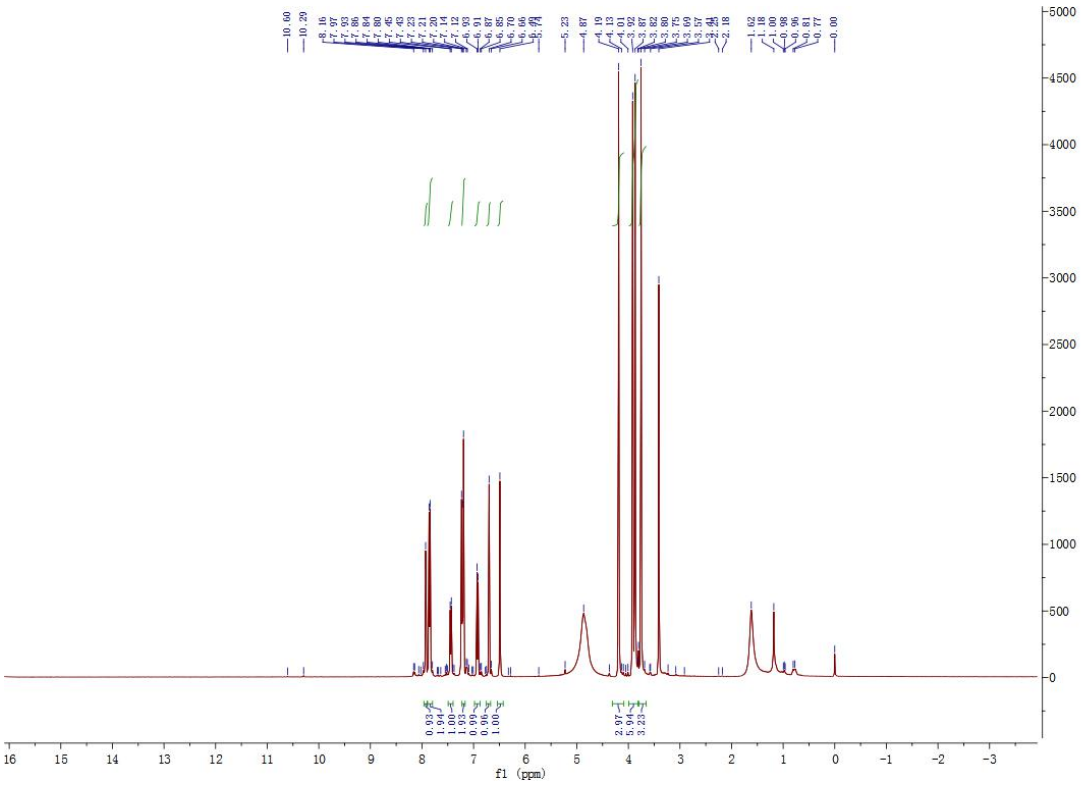


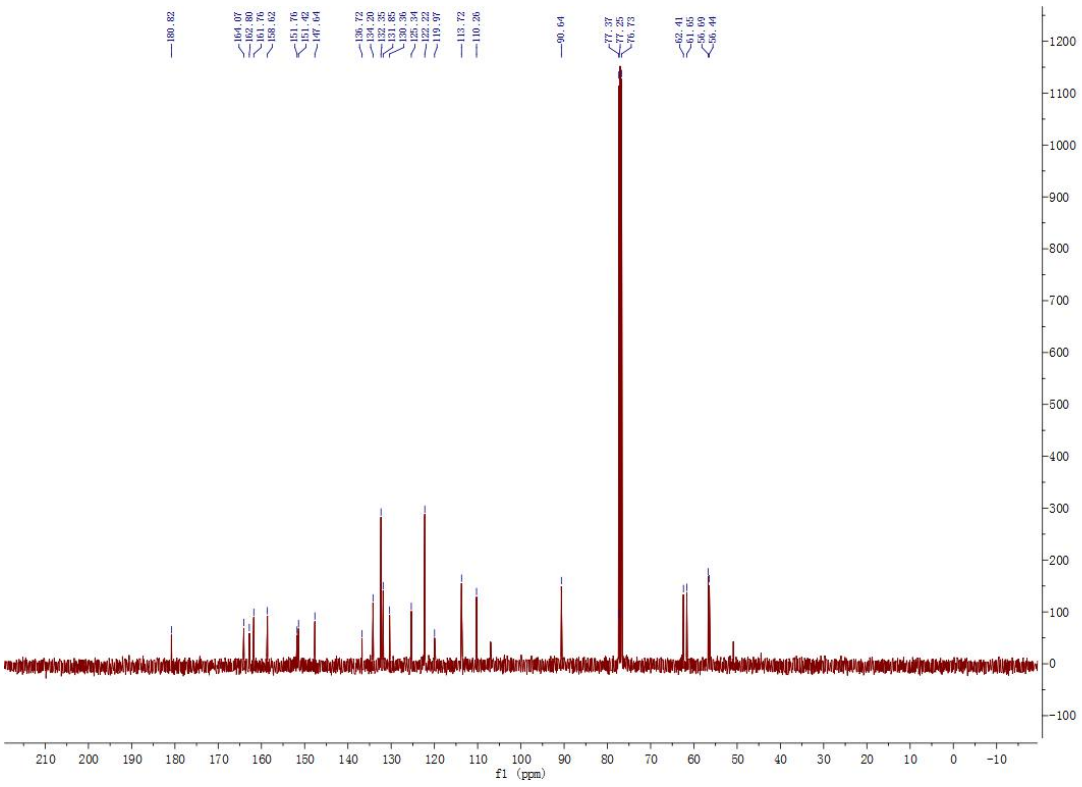




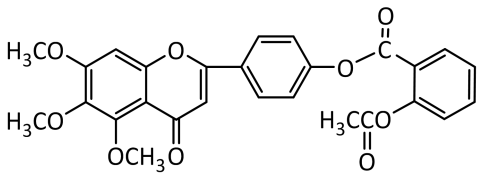
4-(5,6,7-trimethoxy-4-oxo-4H-chromen-2-yl)phenyl5-chloro-2-methoxybenzoate (7e)

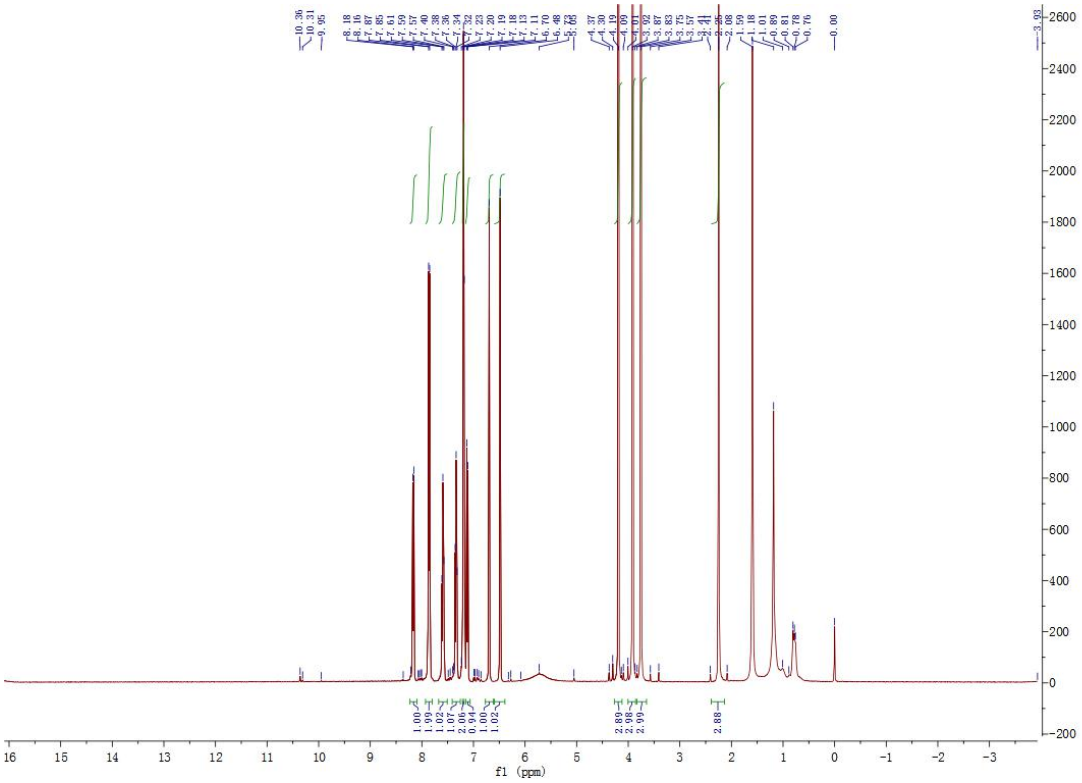


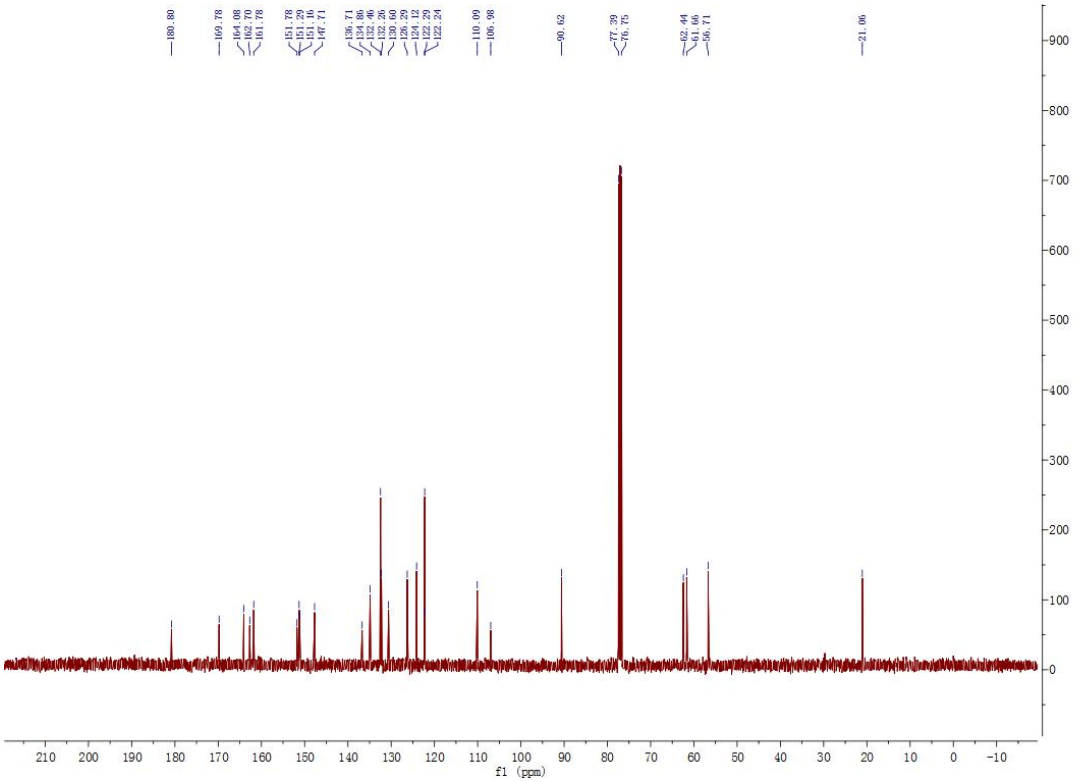




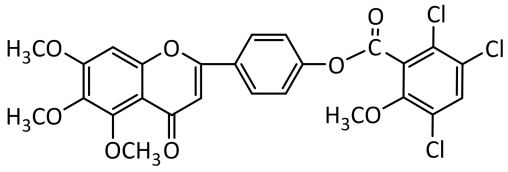
4-(5,6,7-trimethoxy-4-oxo-4H-chromen-2-yl)phenyl 2-acetoxybenzoate (7f)

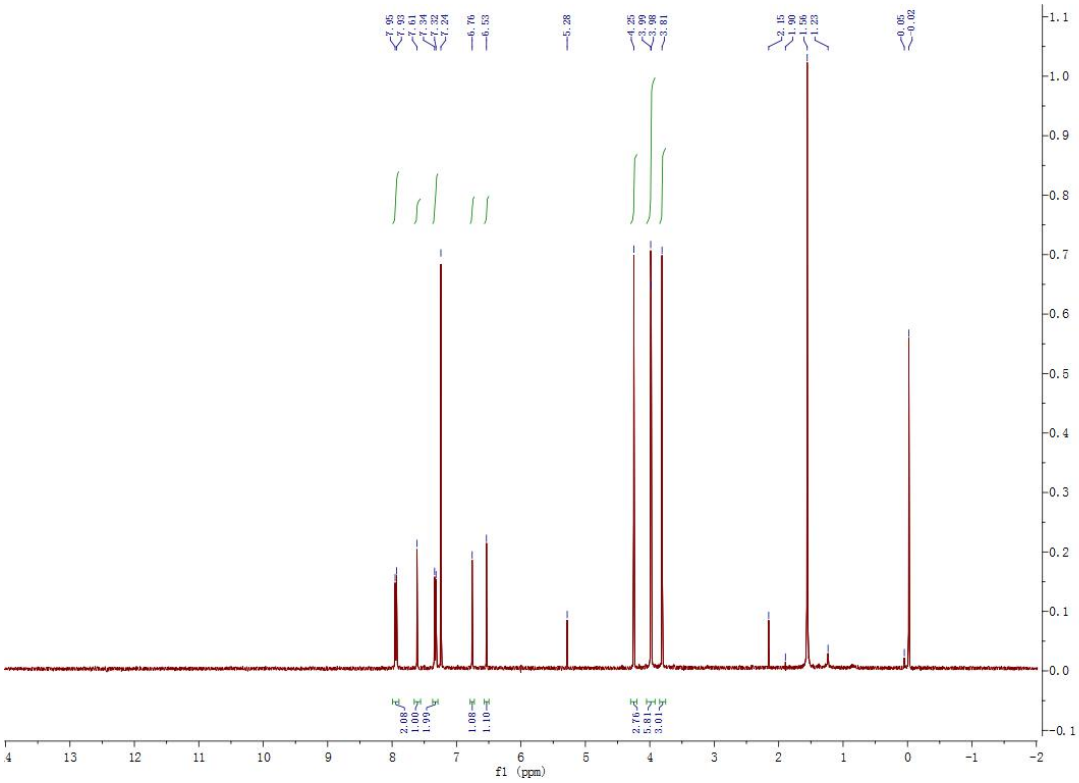


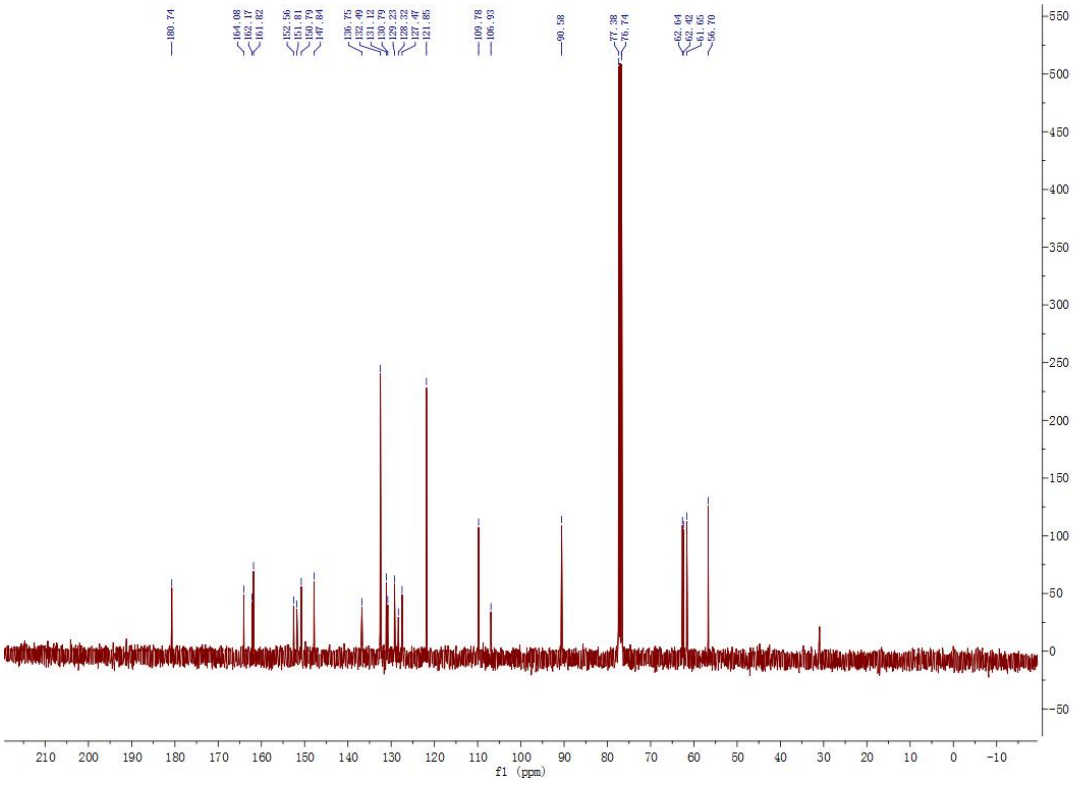




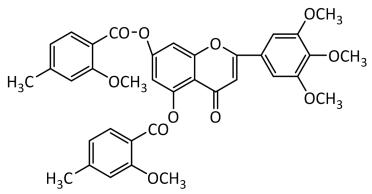
4-(5,6,7-trimethoxy-4-oxo-4H-chromen-2-yl)phenyl 2,3,5-trichloro-6-methoxybenzoate (7g)

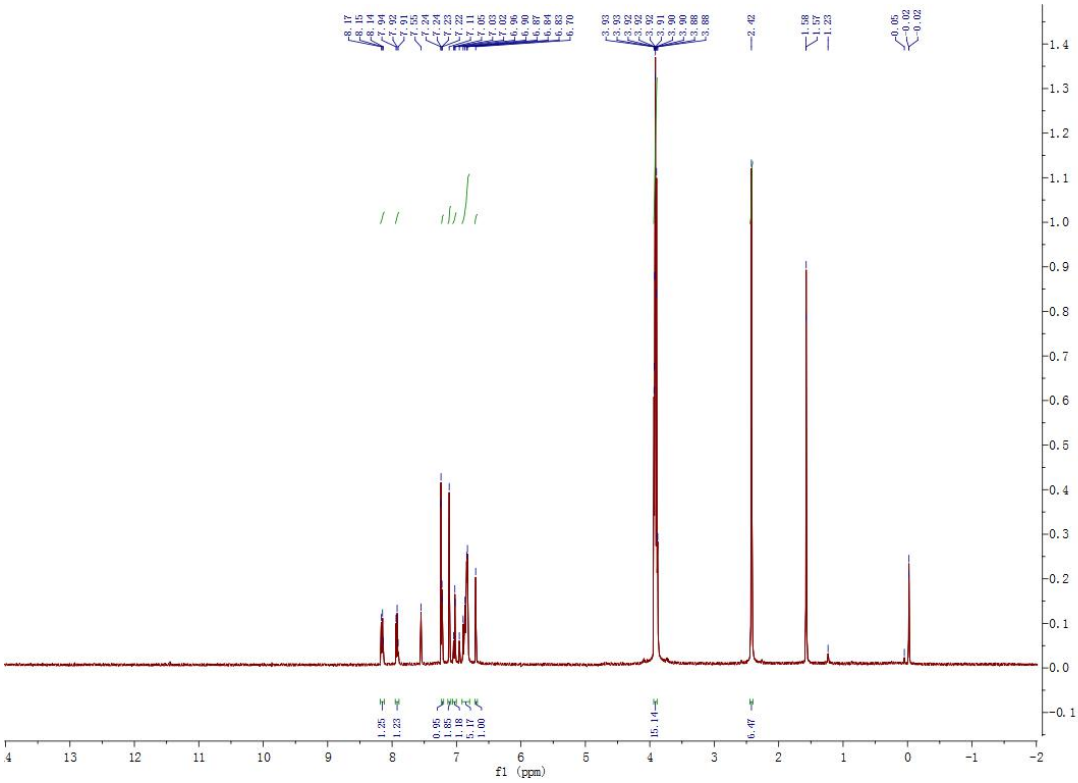


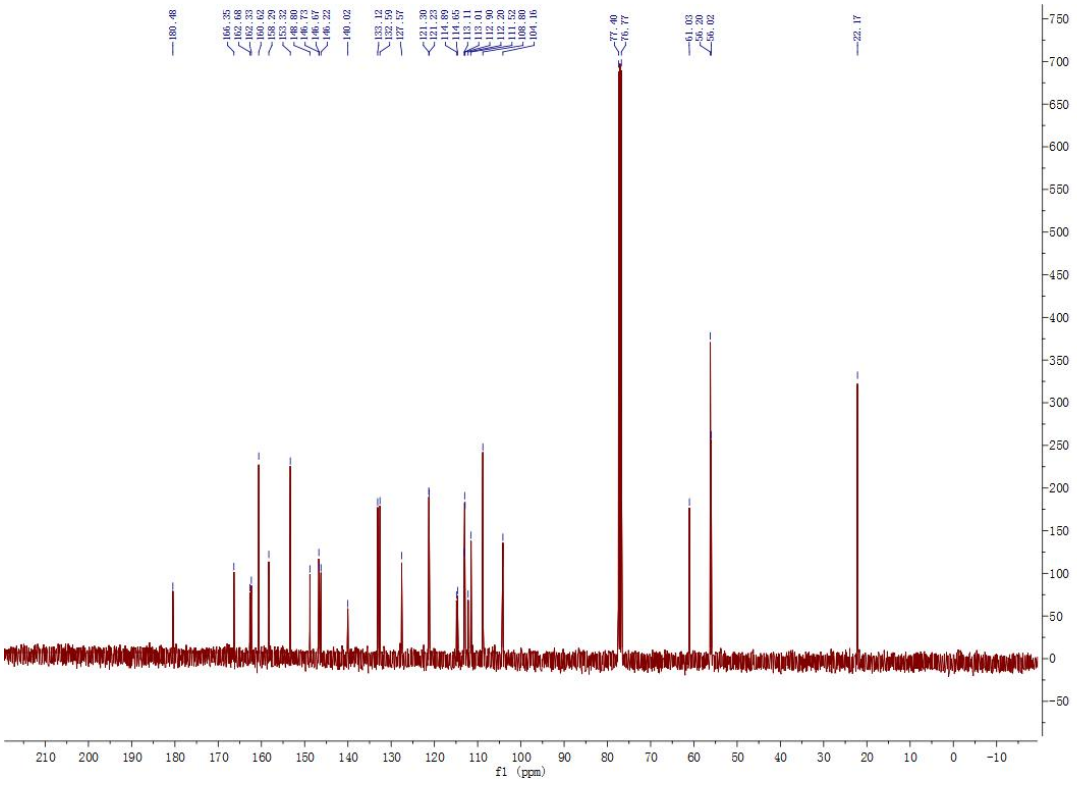




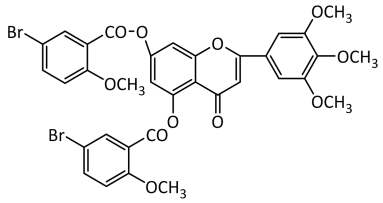
4-oxo-2-(3,4,5-trimethoxyphenyl)-4H-chromene-5,7-diyl bis(2-methoxy-4-methylbenzoate) (8a)

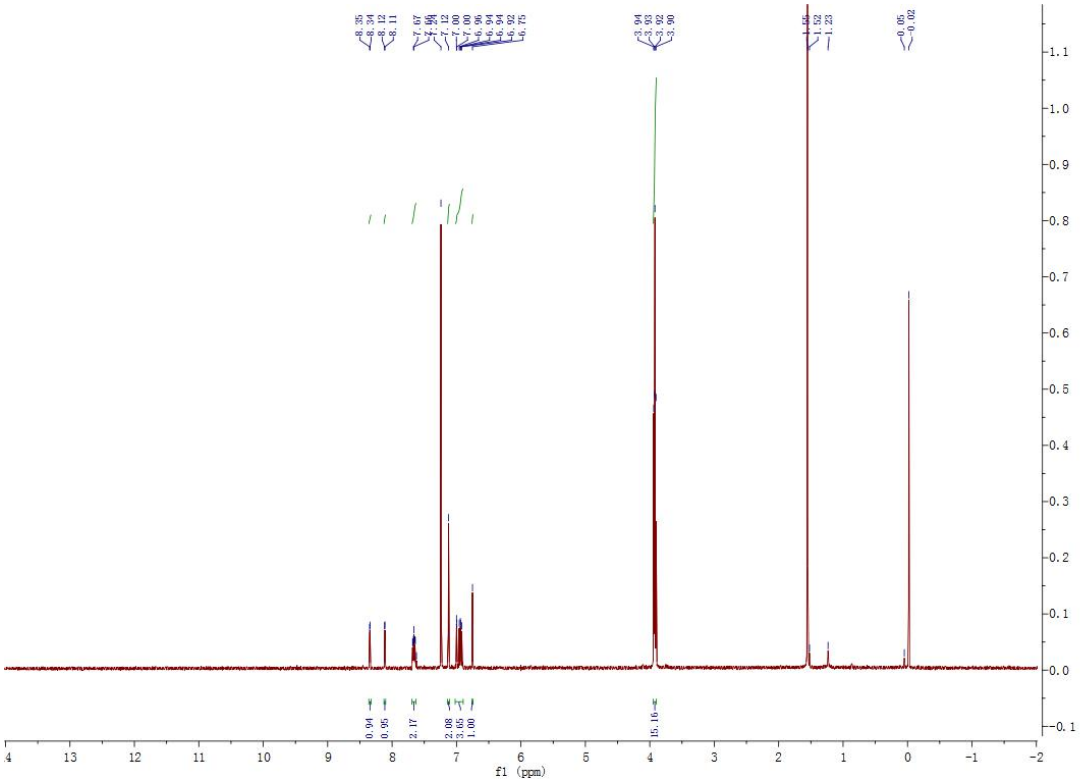


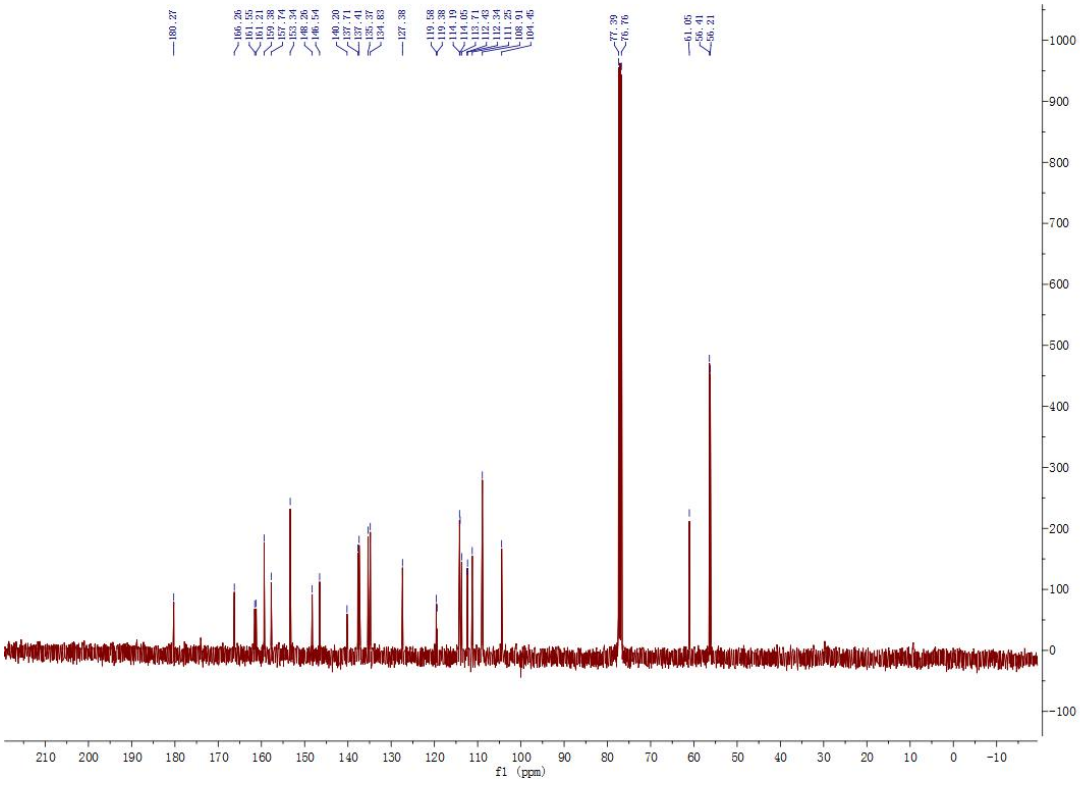




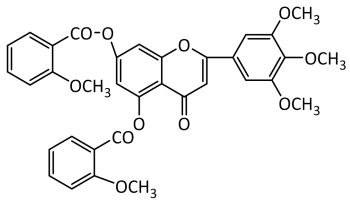
4-oxo-2-(3,4,5-trimethoxyphenyl)-4H-chromene-5,7-diyl bis(5-bromo-2-methoxybenzoate) (8b)

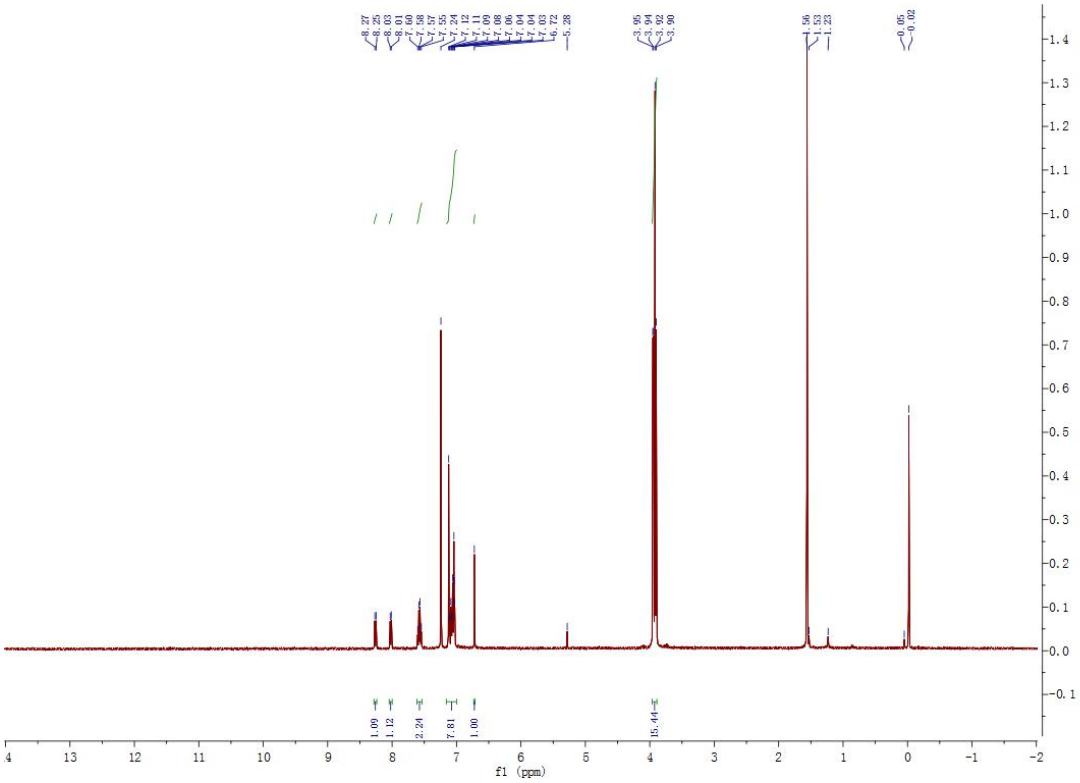


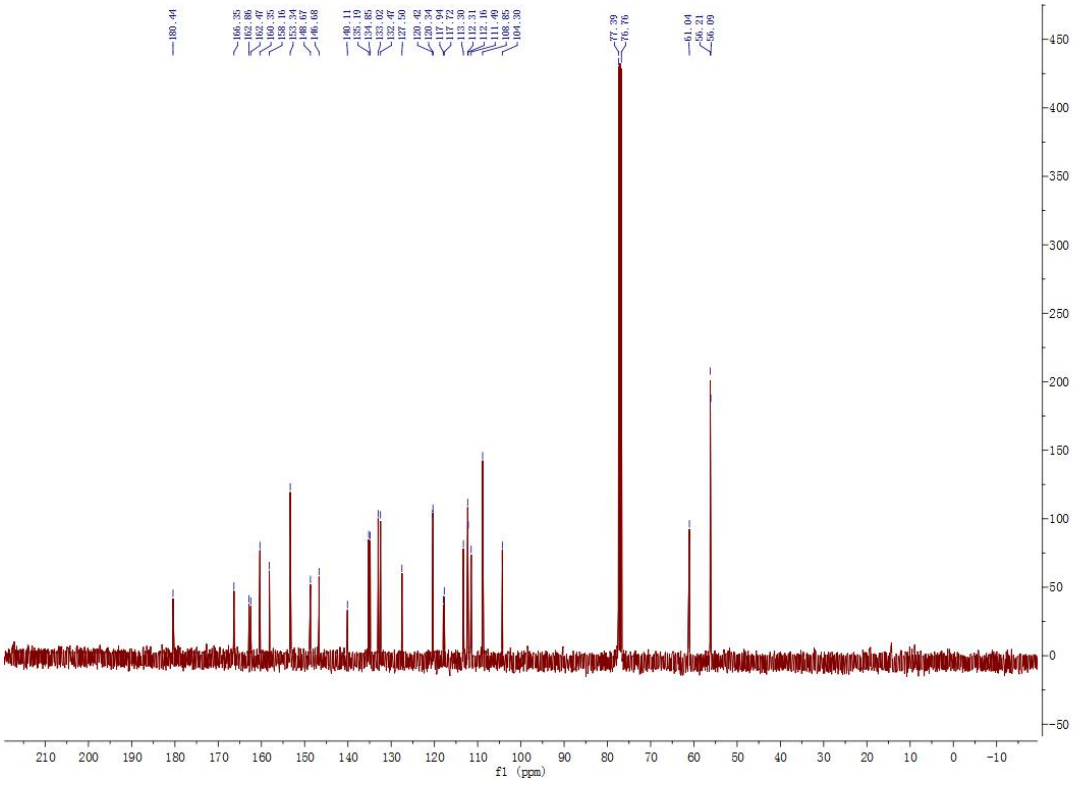




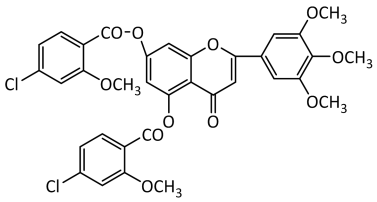
5-(benzoyloxy)-4-oxo-2-(3,4,5-trimethoxyphenyl)-4H-chromen-7-yl 2-methoxybenzoate (8c)

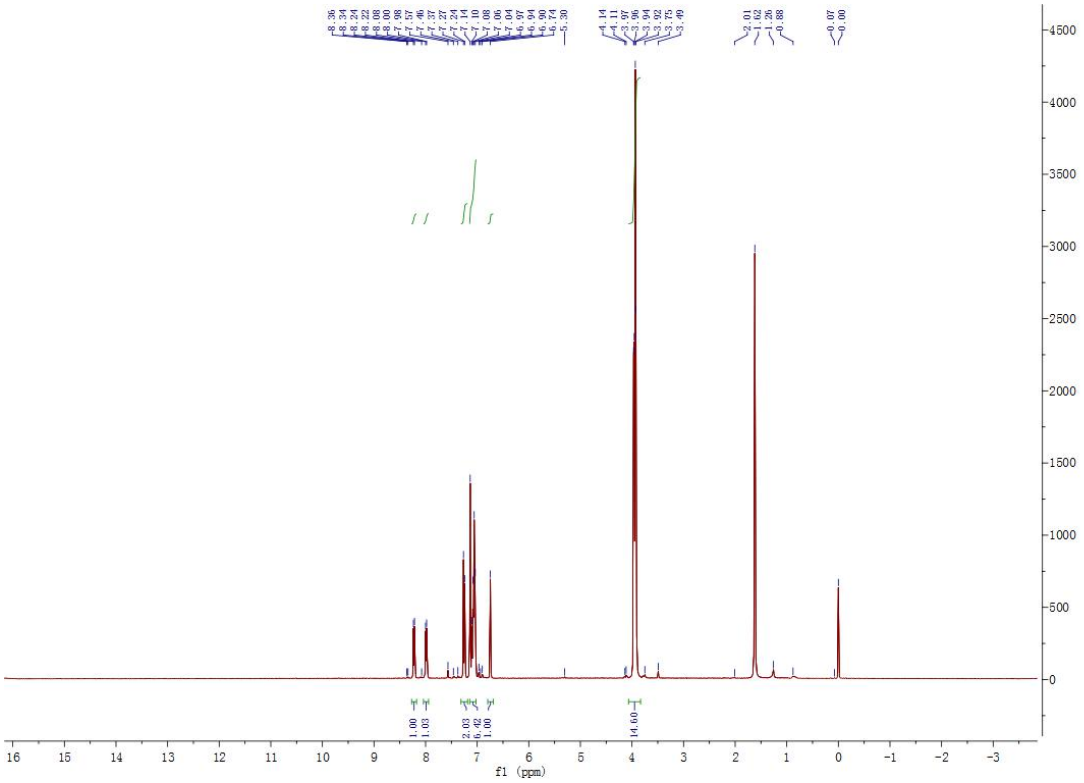


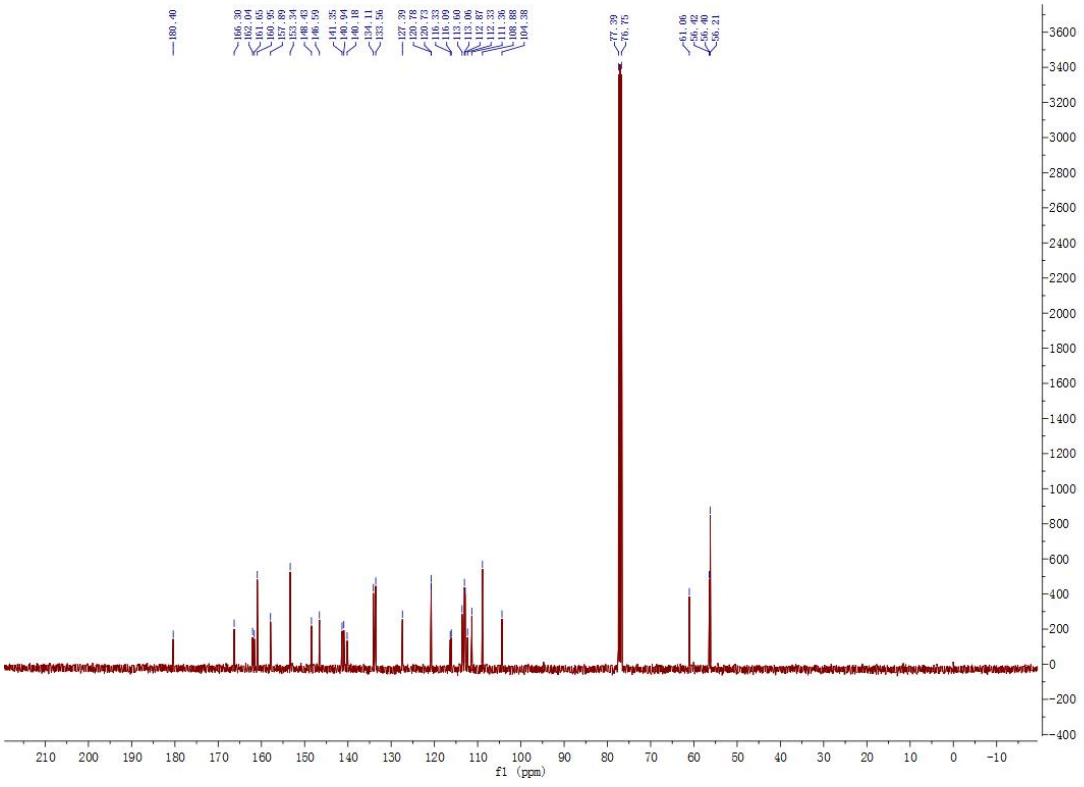




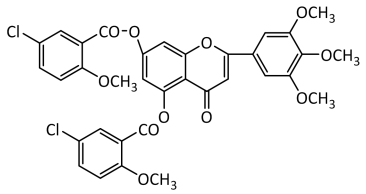
4-oxo-2-(3,4,5-trimethoxyphenyl)-4H-chromene-5,7-diyl bis(4-chloro-2-methoxybenzoate) (8d)

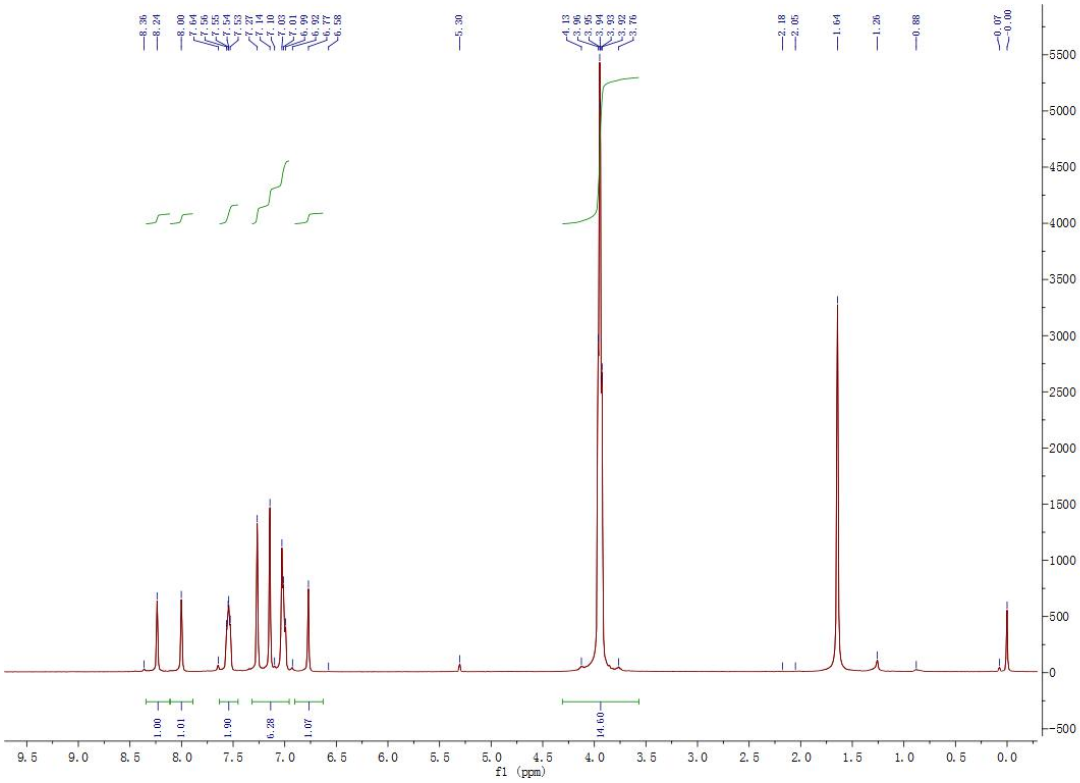


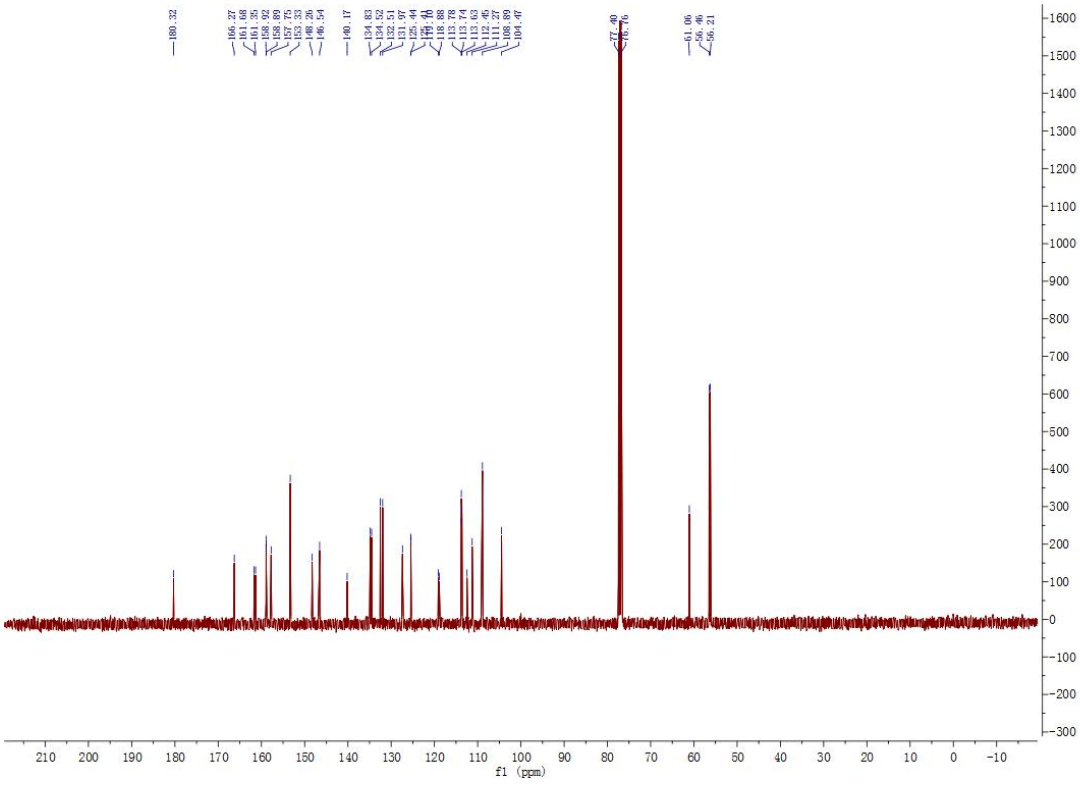




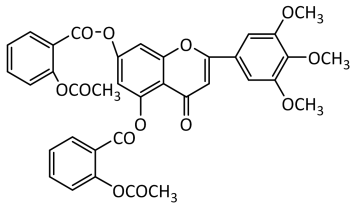
4-oxo-2-(3,4,5-trimethoxyphenyl)-4H-chromene-5,7-diyl bis(5-chloro-2-methoxybenzoate) (8e)

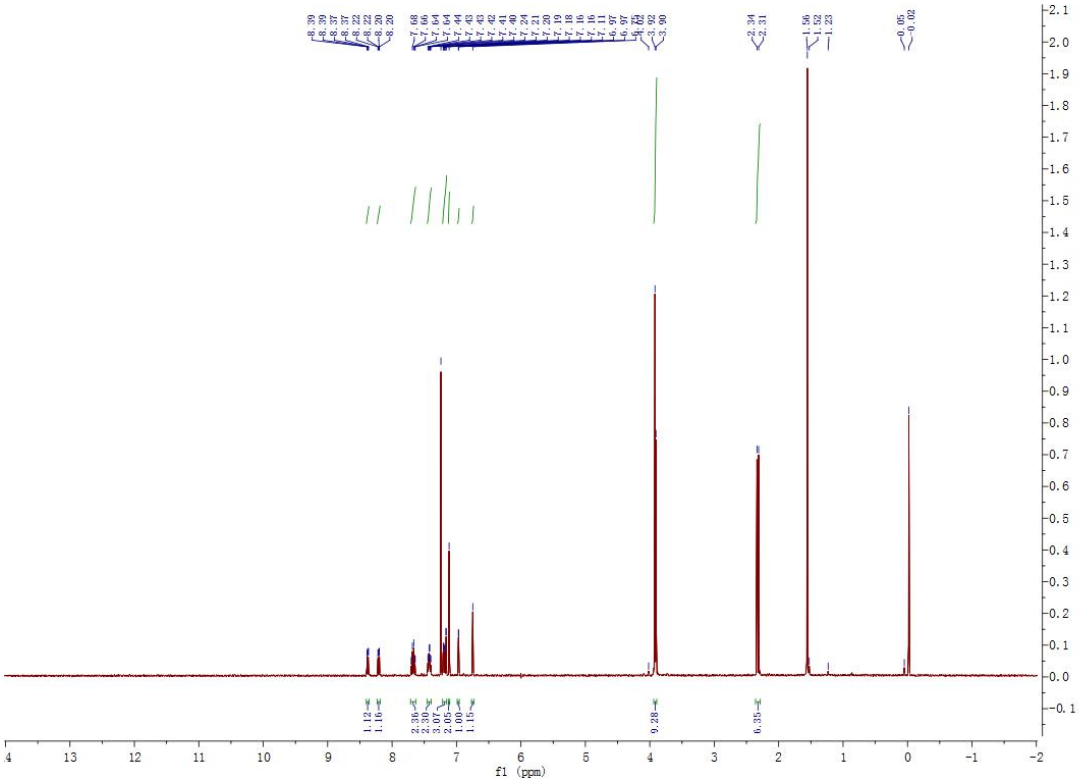


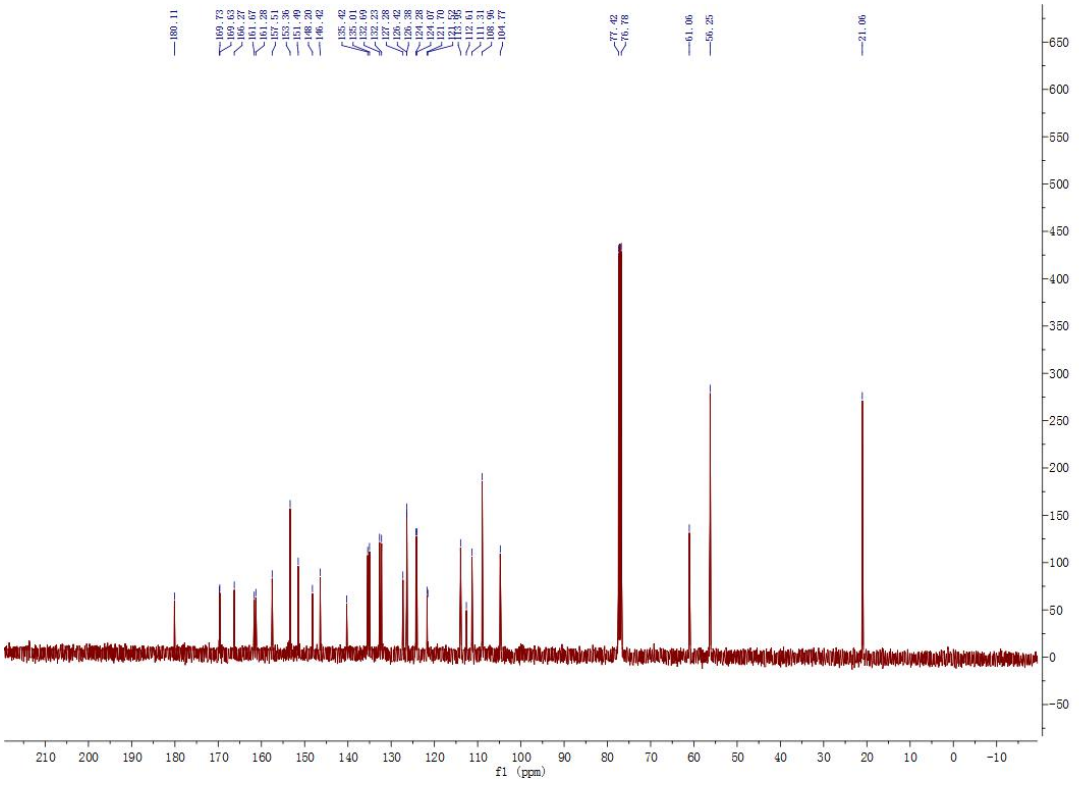




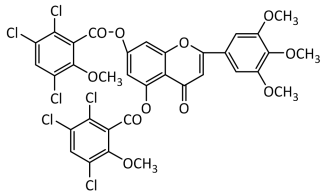
4-oxo-2-(3,4,5-trimethoxyphenyl)-4H-chromene-5,7-diyl bis(2-acetoxybenzoate) (8f)

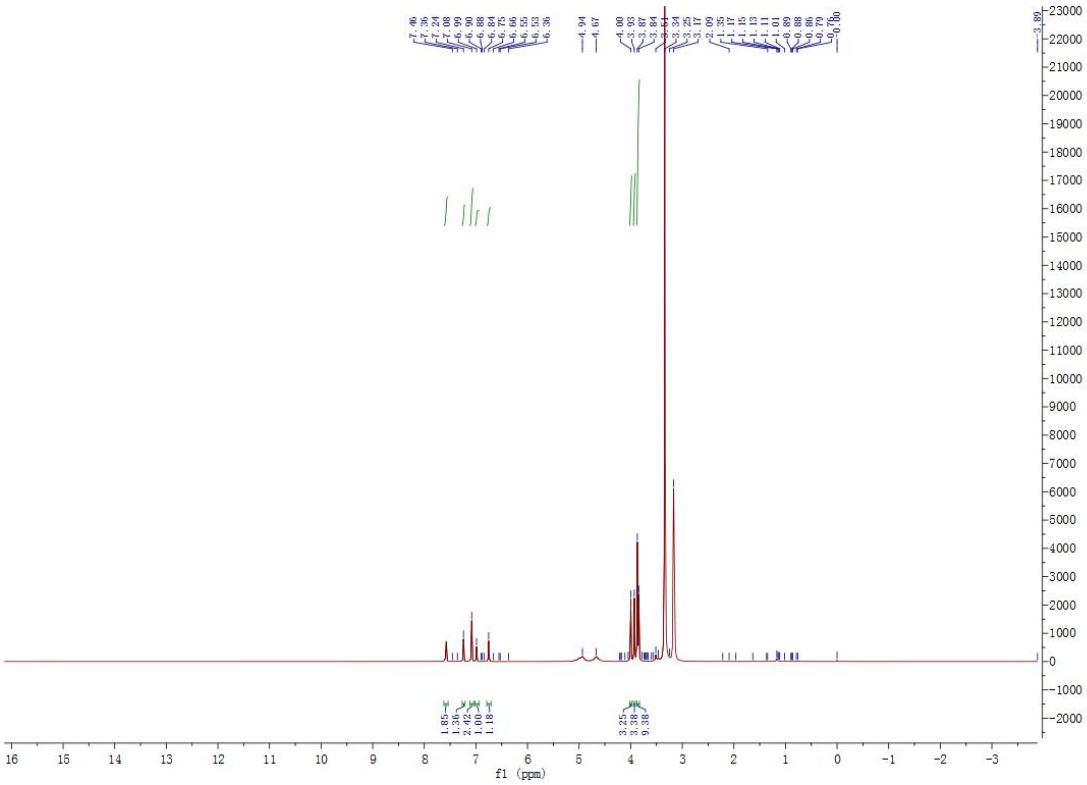


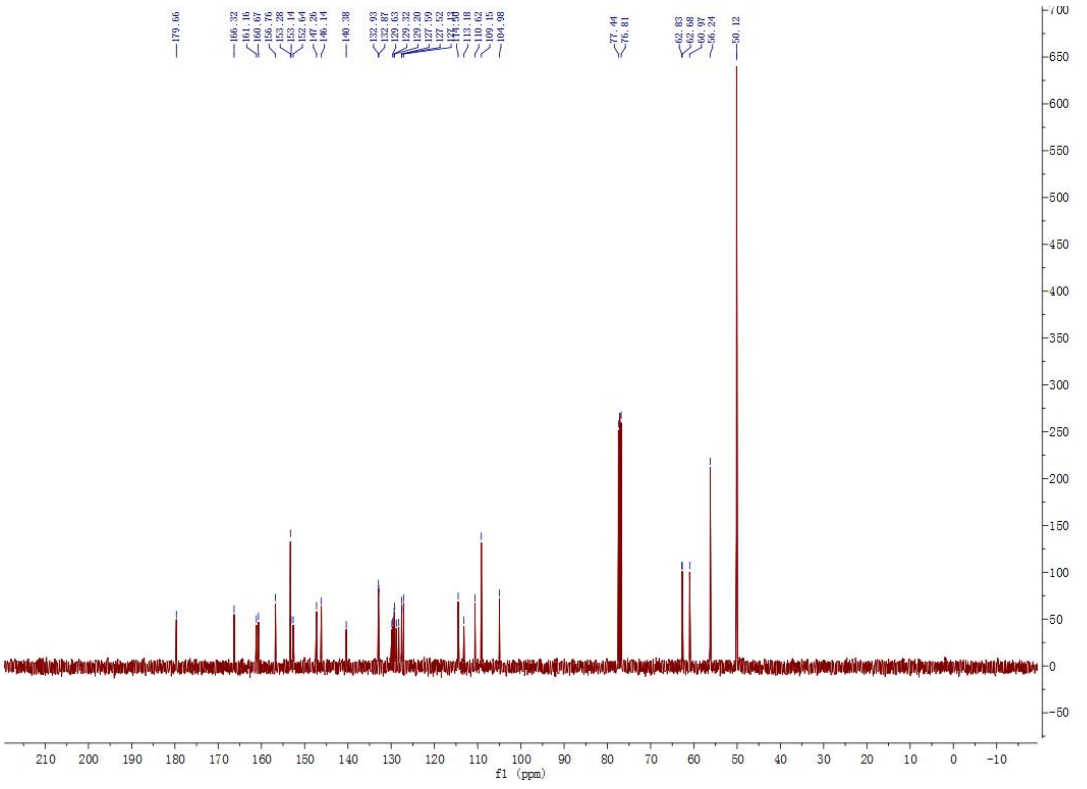




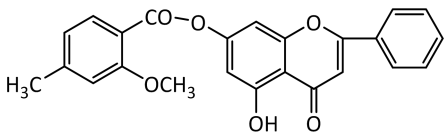
4-oxo-2-(3,4,5-trimethoxyphenyl)-4H-chromene-5,7-diyl bis(2,3,5-trichloro-6-methoxybenzoate) (8g)

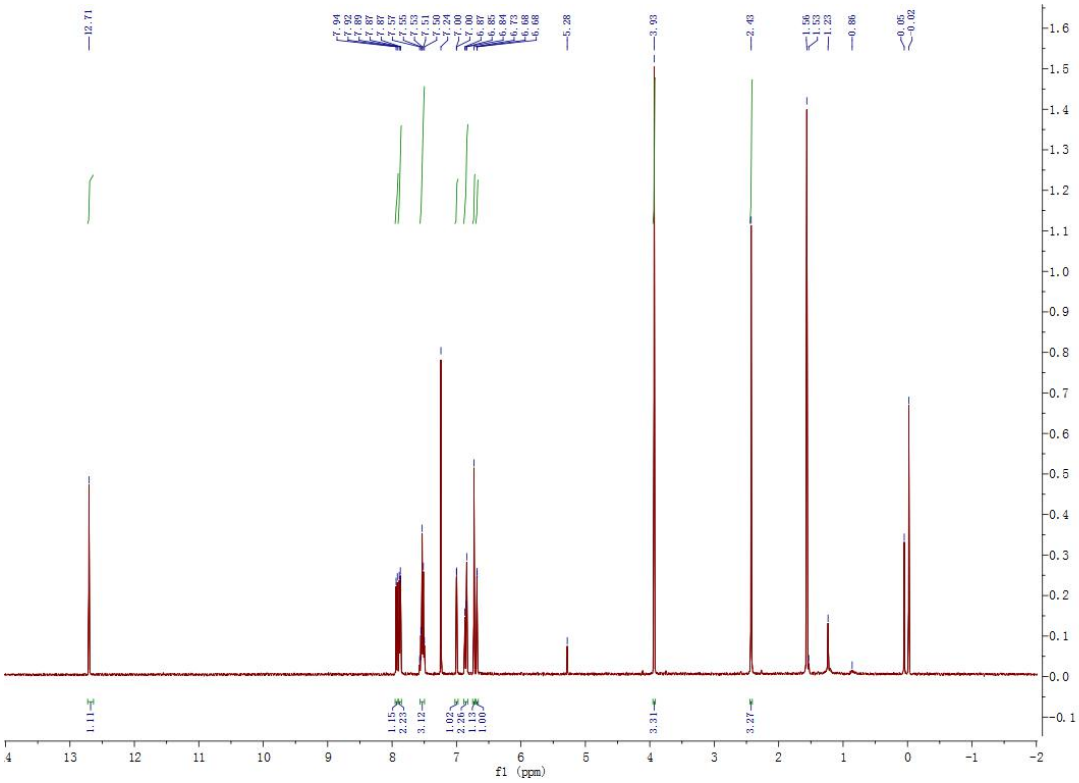


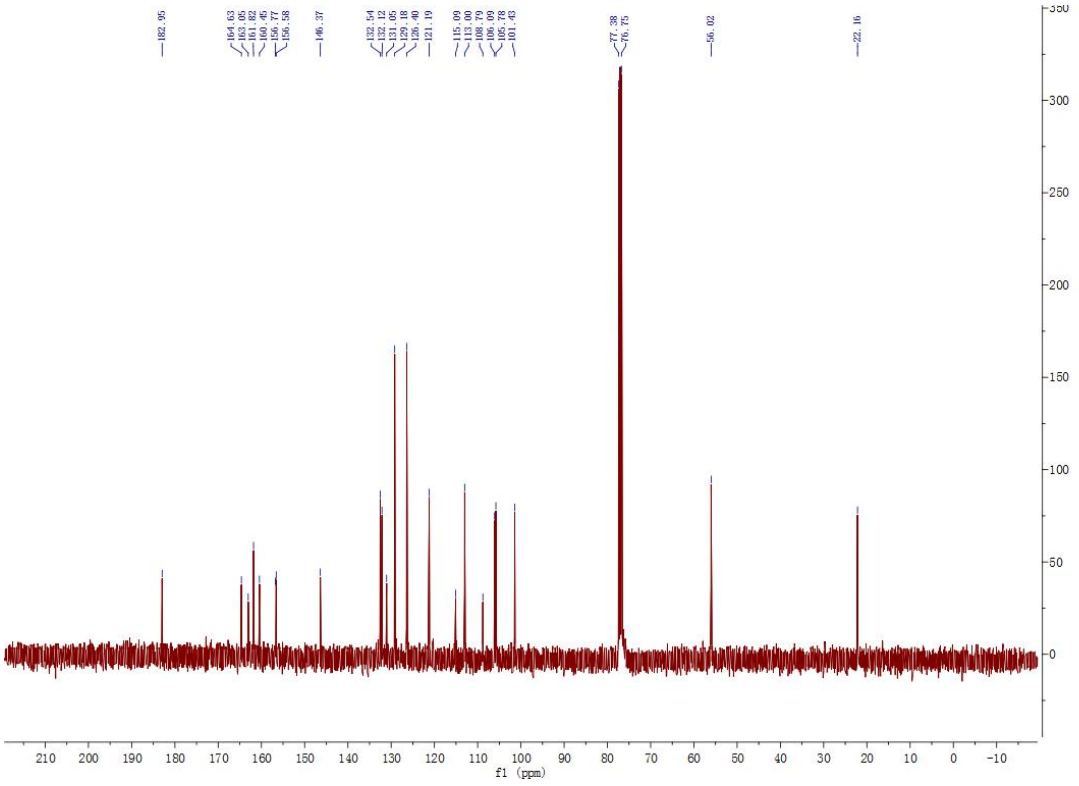




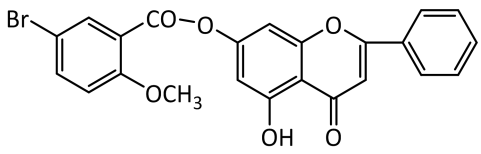
5-hydroxy-4-oxo-2-phenyl-4H-chromen-7-yl 2-methoxy-4-methylbenzoate (9a)

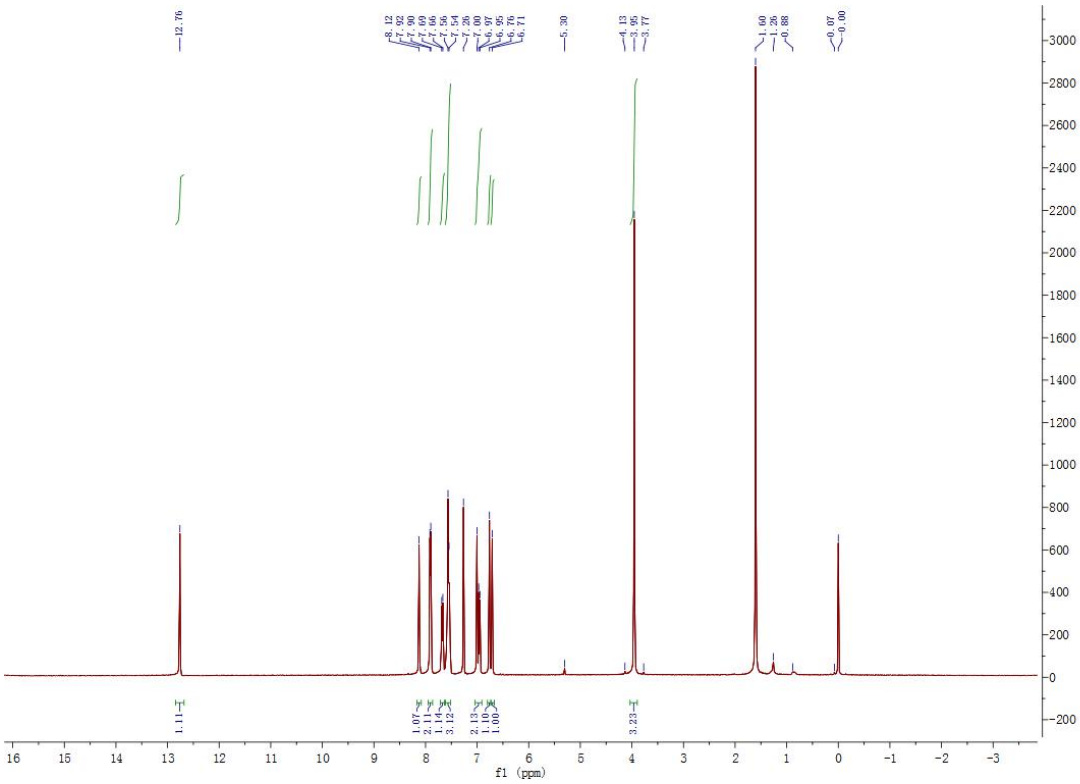


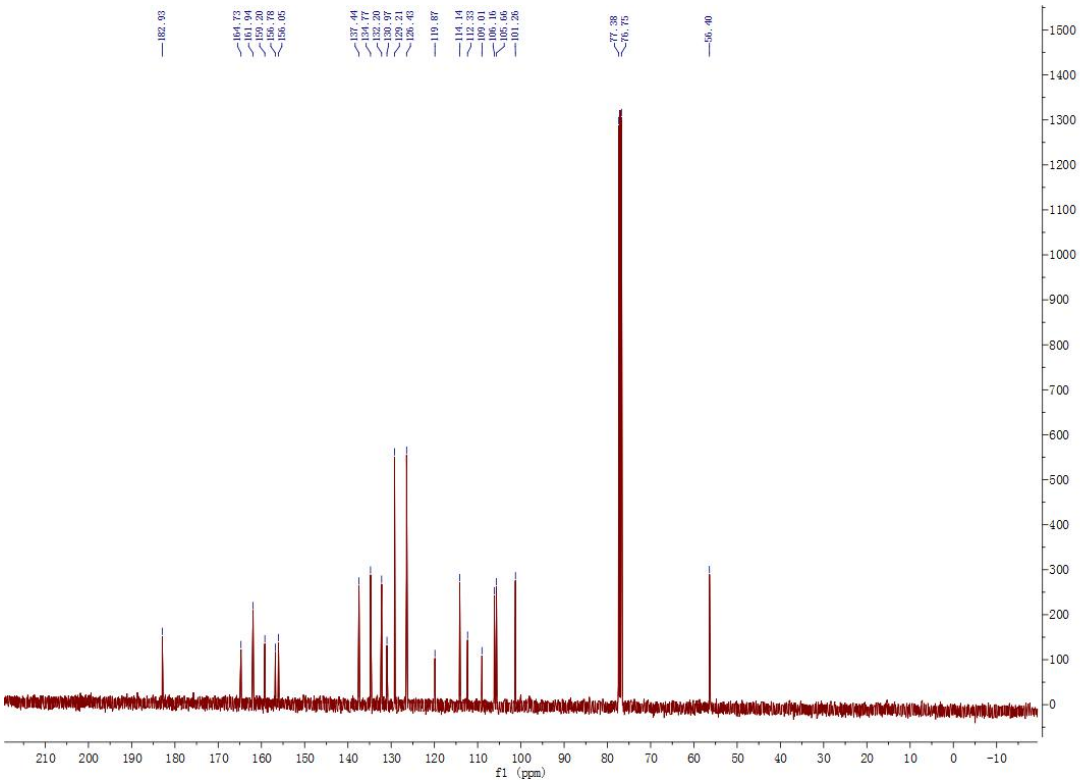




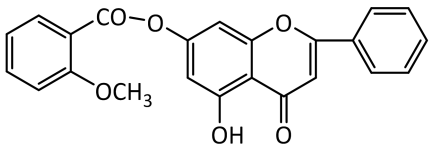
5-hydroxy-4-oxo-2-phenyl-4H-chromen-7-yl 5-bromo-2-methoxybenzoate (9b)

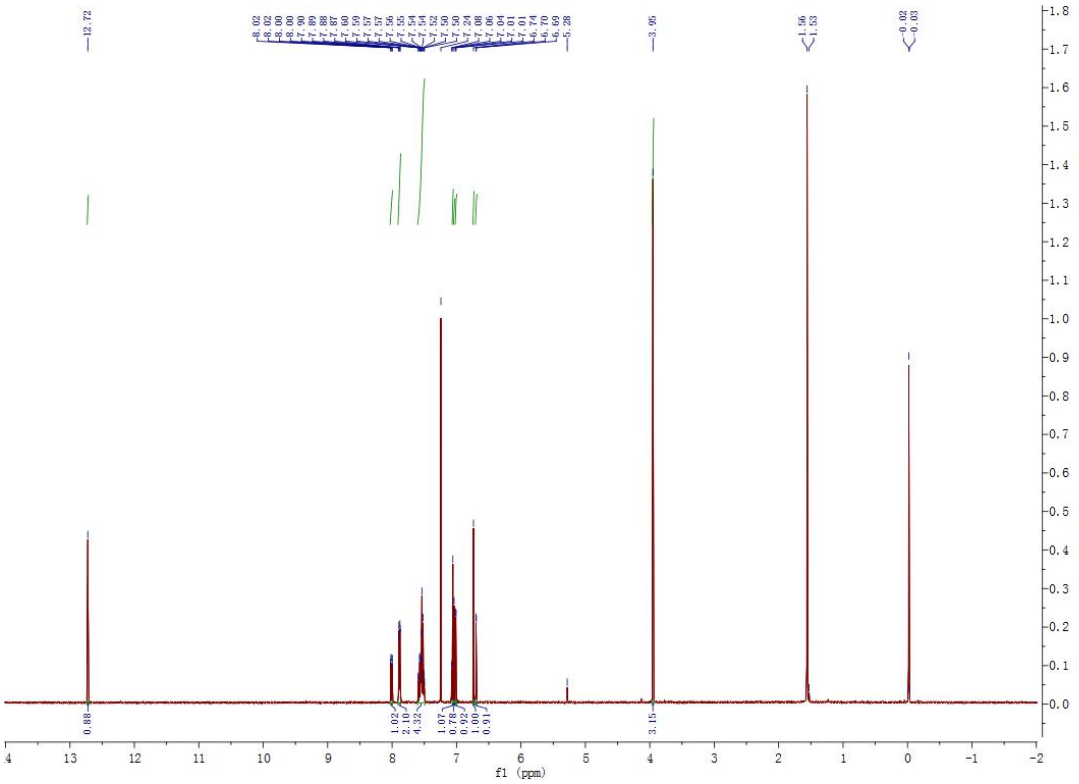


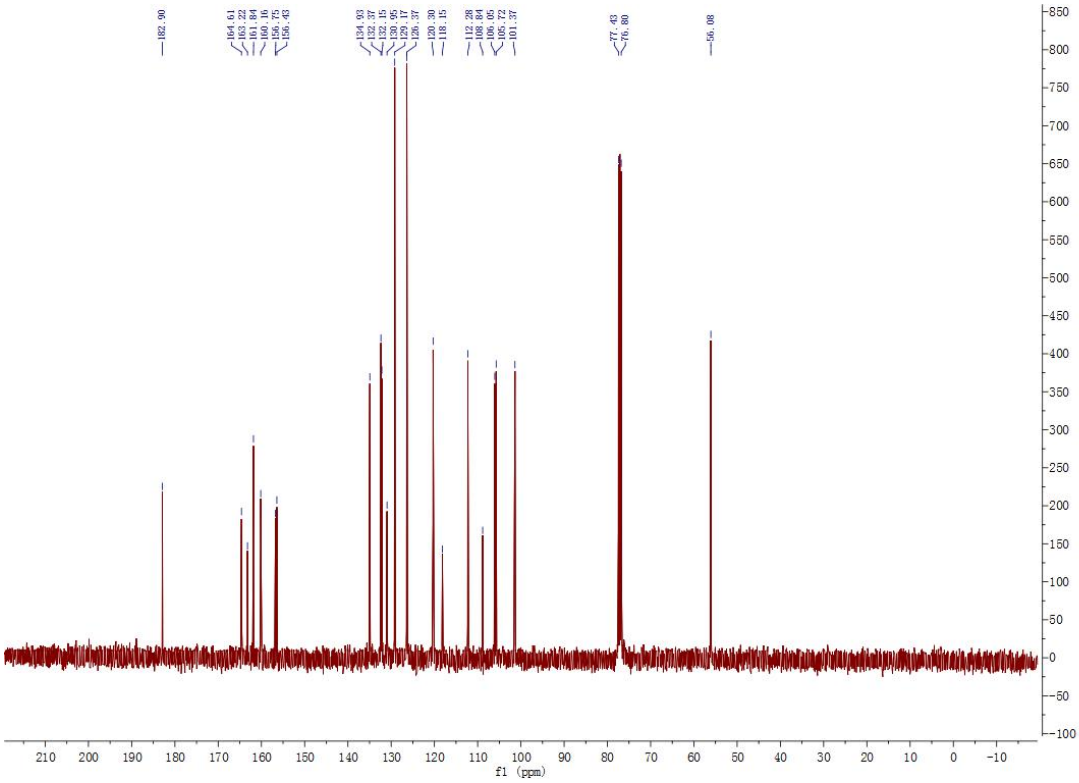




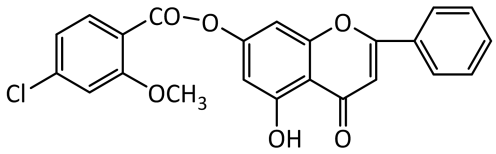
5-hydroxy-4-oxo-2-phenyl-4H-chromen-7-yl 2-methoxybenzoate (9c)

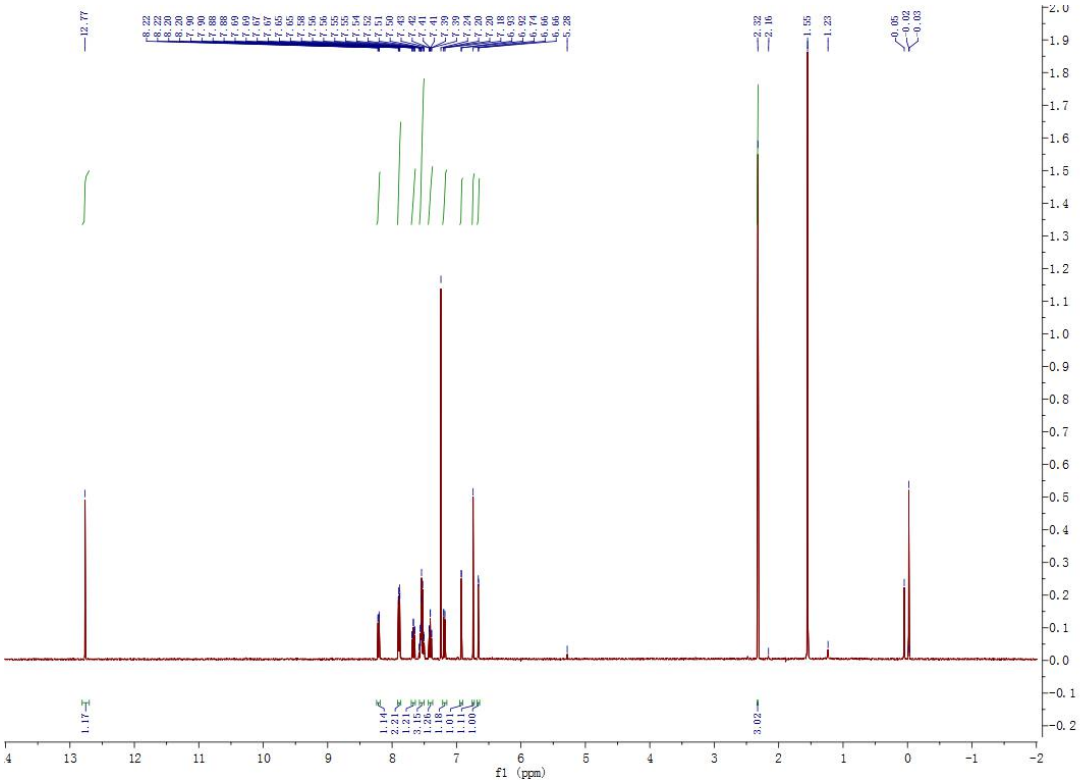


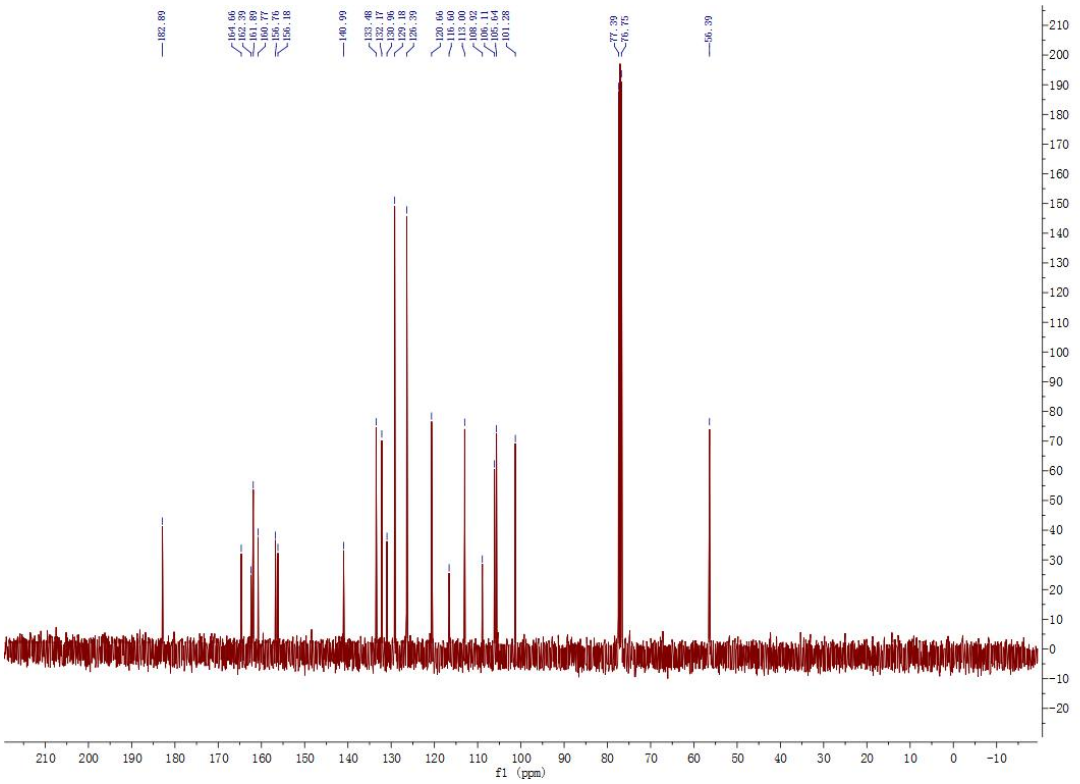




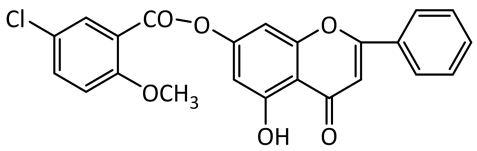
5-hydroxy-4-oxo-2-phenyl-4H-chromen-7-yl 4-chloro-2-methoxybenzoate (9d)

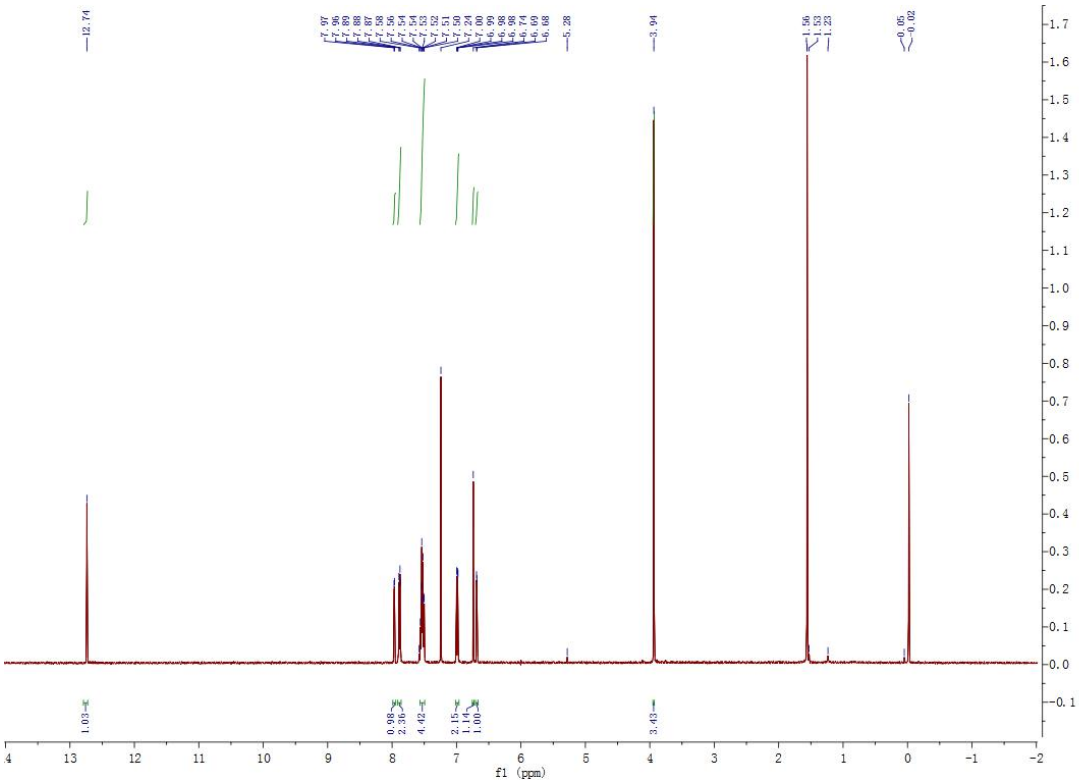


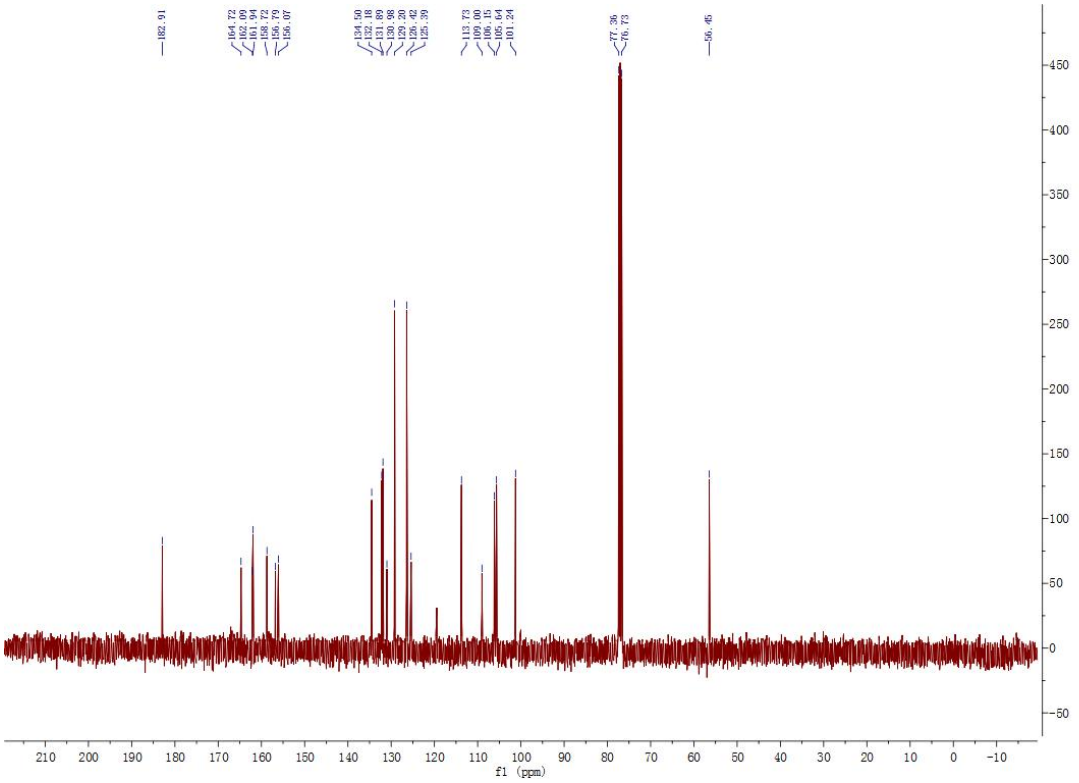




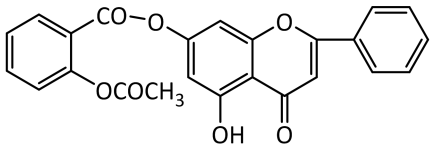
5-hydroxy-4-oxo-2-phenyl-4H-chromen-7-yl 5-chloro-2-methoxybenzoate (9e)

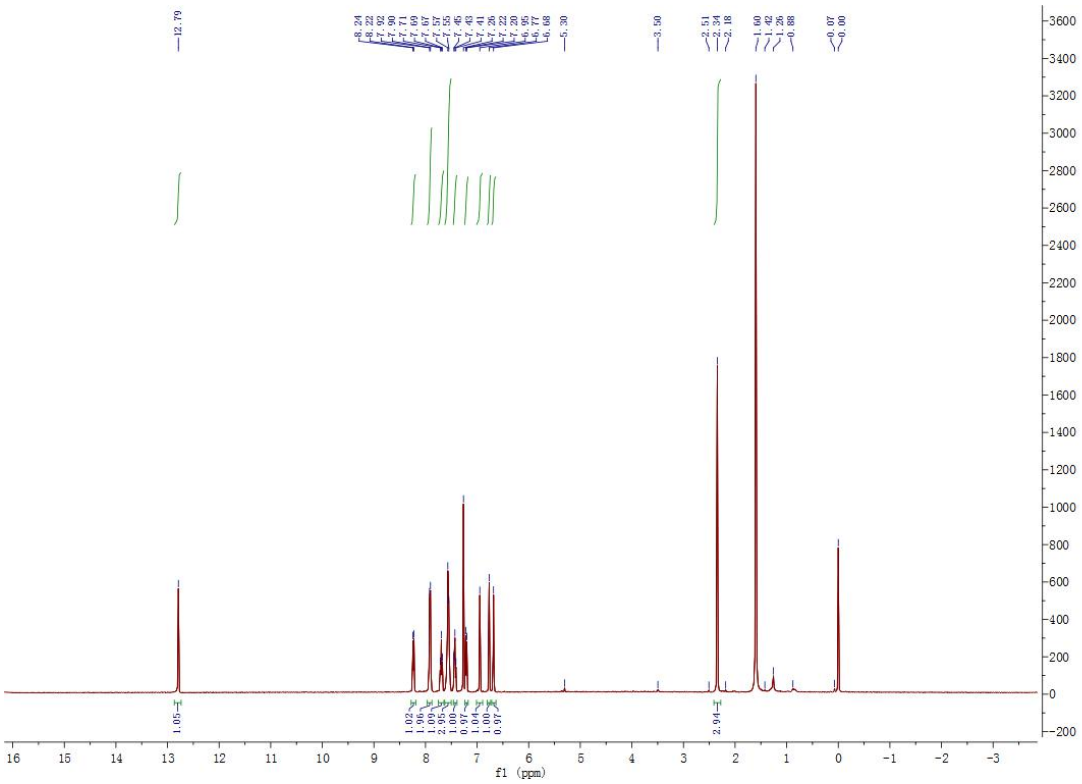


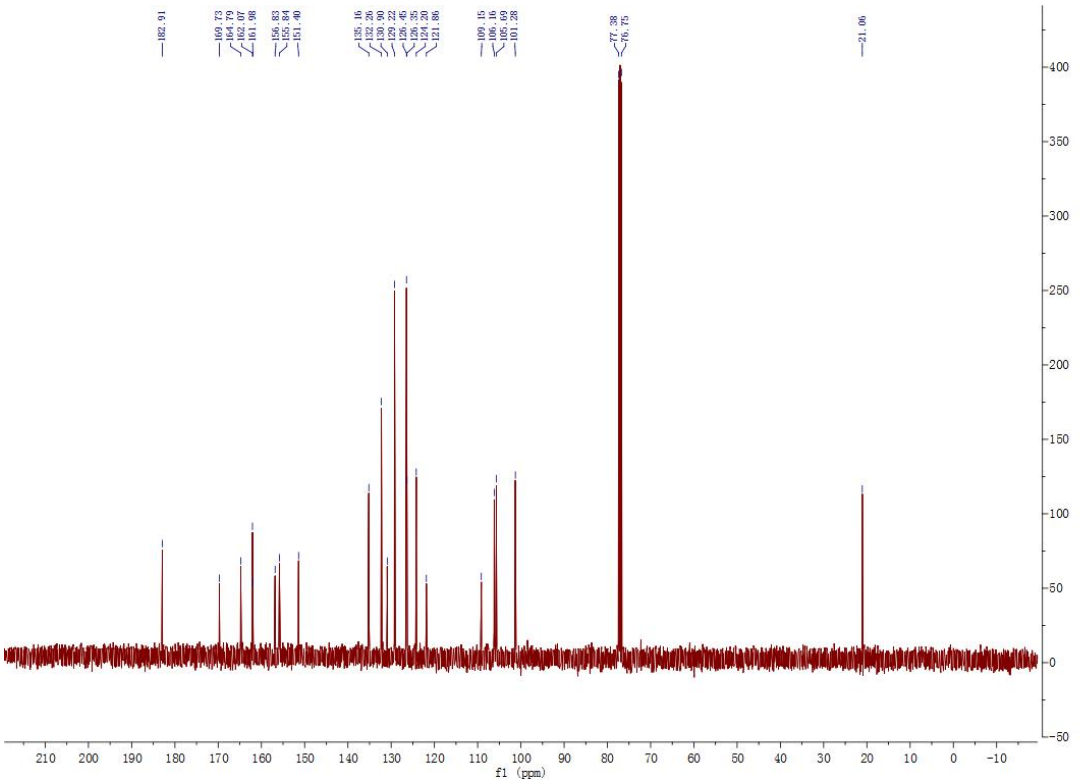




5-hydroxy-4-oxo-2-phenyl-4H-chromen-7-yl 2-acetoxybenzoate (9f)







5-hydroxy-4-oxo-2-phenyl-4H-chromen-7-yl 2,3,5-trichloro-6-methoxybenzoate (9g)